

chain nodes :

10 11

ring nodes :

1 2 3 4 5 6 7 8 9

chain bonds :

8-11 9-10

ring bonds :

1-2 1-7 2-3 3-4 4-5 4-8 5-6 5-9 6-7 8-9

exact/norm bonds :

1-2 1-7 2-3 3-4 4-5 4-8 5-6 5-9 6-7 8-9 8-11 9-10

Match level :

1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:Atom 8:Atom 9:Atom 10:CLASS
11:CLASS

/

10/820,215

=> d his

(FILE 'HOME' ENTERED AT 11:23:58 ON 17 FEB 2006)

FILE 'REGISTRY' ENTERED AT 11:24:06 ON 17 FEB 2006

L1 1 S 144912-63-0/RN

FILE 'CAPLUS' ENTERED AT 11:24:16 ON 17 FEB 2006

L2 18 S L1

L3 4883 S INTRANASAL

L4 1 S L2 AND L3

=> d ibib abs hitstr total l2

L2 ANSWER 1 OF 18 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2005:572349 CAPLUS

DOCUMENT NUMBER: 143:103227

TITLE: Oral administration of [2-(8,9-dioxo-2,6-diazabicyclo[5.2.0]non-1(7)-en-2-yl)alkyl] phosphonic acid and derivatives

INVENTOR(S): Benjamin, Eric J.; Cloud, William F.; Ashraf, Muhammad; Islam, Mohammed; Brandt, Michael R.; Tremblay, Gerald F.

PATENT ASSIGNEE(S): Wyeth, John, and Brother Ltd., USA

SOURCE: U.S. Pat. Appl. Publ., 32 pp.

CODEN: USXXCO

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 4

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------------------------|------|----------|-----------------|------------|
| US 2005142192 | A1 | 20050630 | US 2004-961871 | 20041008 |
| US 2005004079 | A1 | 20050106 | US 2004-820215 | 20040407 |
| US 2005004080 | A1 | 20050106 | US 2004-820216 | 20040407 |
| PRIORITY APPLN. INFO.: | | | US 2003-511560P | P 20031015 |
| | | | US 2004-820215 | A 20040407 |
| | | | US 2004-820216 | A 20040407 |
| | | | US 2003-461490P | P 20030409 |
| | | | US 2003-461571P | P 20030409 |

OTHER SOURCE(S): MARPAT 143:103227

AB Solid, pharmaceutical dosage forms of [2-(8,9-dioxo-2,6-diazabicyclo[5.2.0]non-1(7)-en-2-yl)alkyl]phosphonic acid and derivs. thereof are disclosed. In addition, methods of use are disclosed for the treatment, inter alia, of cerebral vascular disorders, anxiety disorders; mood disorders; schizophrenia; schizophreniform disorder; schizoaffective disorder; cognitive impairment; chronic neurodegenerative disorders; inflammatory diseases; fibromyalgia; complications from herpes zoster; prevention of tolerance to opiate analgesia; withdrawal symptoms from addictive drugs; and pain. For example, enteric coated tablets contained [2-(8,9-dioxo-2,6-diazabicyclo[5.2.0]non-1(7)-en-2-yl)ethyl] phosphonic acid 200, croscarmellose sodium 7.05, Povidone 3.53, Avicel PH101 14.1, croscarmellose sodium 4.7, sodium lauryl sulfate 5.88 and magnesium stearate 1.18 mg.

IT 144912-63-0

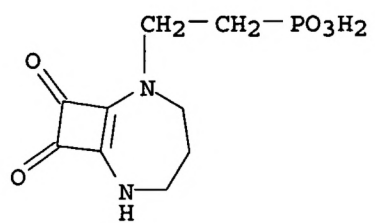
RL: PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(oral administration of [2-(8,9-dioxo-2,6-diazabicyclo[5.2.0]non-1(7)-en-2-yl)alkyl] phosphonic acid and derivs. for the treatment of mental disorders and inflammatory diseases and pain relief)

RN 144912-63-0 CAPLUS

CN Phosphonic acid, [2-(8,9-dioxo-2,6-diazabicyclo[5.2.0]non-1(7)-en-2-yl)ethyl]- (9CI) (CA INDEX NAME)

10/820,215



LA ANSWER 2 OF 18 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2005:510827 CAPLUS

DOCUMENT NUMBER: 143:109575

TITLE: Pharmacological characterization of antiepileptic drugs and experimental analgesics on low magnesium-induced hyperexcitability in rat hippocampal slices

AUTHOR(S): Arias, Robert L.; Bowlby, Mark R.

CORPORATE SOURCE: Discovery Neuroscience, Wyeth Research, Princeton, NJ, 08543-8000, USA

SOURCE: Brain Research (2005), 1047(2), 233-244

CODEN: BRREAP; ISSN: 0006-8993

PUBLISHER: Elsevier B.V.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Perfusion of acute hippocampal slices with stimulatory buffers has long been known to induce rhythmic, large amplitude, synchronized spontaneous neuronal bursting in areas CA1 and CA3. The characteristics of this model of neuronal hyperexcitability were investigated in this study, particularly with respect to the activity of antiepileptic drugs and compds. representing novel mechanisms of analgesic action. Toward that end, low Mg²⁺/high K⁺-induced spontaneous activity was quantified by a virtual instrument designed for the digitization and anal. of bursting activity. Uninterrupted streams of extracellular field potentials were digitized and analyzed in 10-s sweeps, yielding four quantified parameters of neuronal hyperexcitability. Following characterization of the temporal stability of low Mg²⁺/high K⁺-induced hyperexcitability, compds. representing a diversity of functional mechanisms were tested for their effectiveness in reversing this activity. Of the four antiepileptic drugs tested in this model, only phenytoin proved ineffective, while valproate, gabapentin and carbamazepine varied in their potencies, with only the latter drug proving to be completely efficacious. In addition, three investigational compds. having analgesic potential were examined: ZD-7288, a blocker of HCN channels; EAA-090, an NMDA antagonist; and WAY-132983, a muscarinic agonist. Each of these compds. showed strong efficacy by completely blocking spontaneous bursting activity, along with potency greater than that of the antiepileptic drugs. These data indicate that pharmacol. agents with varying mechanisms of action are able to block low Mg²⁺/high K⁺-induced hyperexcitability, and thus this model may represent a useful tool for identifying novel agents and mechanisms involved in epilepsy and neuropathic pain.

IT 144912-63-0, EAA-090

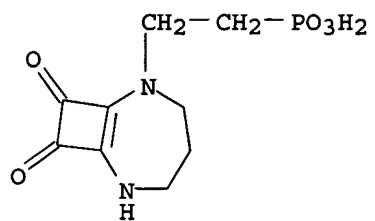
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(pharmacol. characterization of antiepileptic drugs and exptl. analgesics on low magnesium-induced hyperexcitability in rat hippocampal slices)

RN 144912-63-0 CAPLUS

CN Phosphonic acid, [2-(8,9-dioxo-2,6-diazabicyclo[5.2.0]non-1(7)-en-2-yl)ethyl]- (9CI) (CA INDEX NAME)

10/820,215



REFERENCE COUNT:

55

THERE ARE 55 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

12 ANSWER 3 OF 18 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2005:473790 CAPLUS

DOCUMENT NUMBER: 143:71625

TITLE: Effects of the N-methyl-D-aspartate receptor antagonist perzinfotel [EAA-090; [2-(8,9-dioxo-2,6-diazabicyclo[5.2.0]non-1(7)-en-2-yl)-ethyl]phosphonic acid] on chemically induced thermal hypersensitivity

AUTHOR(S): Brandt, Michael R.; Cummons, Terri A.; Potestio, Lisa; Sukoff, Stacey J.; Rosenzweig-Lipson, Sharon

CORPORATE SOURCE: Neuroscience Discovery Research, Wyeth Research, Princeton, NJ, USA

SOURCE: Journal of Pharmacology and Experimental Therapeutics (2005), 313(3), 1379-1386
CODEN: JPETAB; ISSN: 0022-3565

PUBLISHER: American Society for Pharmacology and Experimental Therapeutics

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Perzinfotel [EAA-090; [2-(8,9-dioxo-2,6-diazabicyclo[5.2.0]non-1(7)-en-2-yl)-ethyl]phosphonic acid] is a selective, competitive N-methyl-D-aspartate (NMDA) receptor antagonist with high affinity for the glutamate site. The current study evaluated whether perzinfotel would have antinociceptive effects or block thermal hypersensitivity associated with the administration of chemical irritants in rats. Perzinfotel lacked antinociceptive effects but dose- and time-dependently blocked prostaglandin E2 (PGE2)- and capsaicin-induced thermal hypersensitivity in a warm-water tail-withdrawal assay in rats. Doses of 10 mg/kg i.p. or 100 mg/kg oral blocked PGE2-induced hypersensitivity by 60 to 80%. The magnitude of reversal was greater than other neg. modulators of the NMDA receptor studied, such as uncompetitive channel blockers (e.g., memantine, dizocilpine, and ketamine), a NR2B selective antagonist (e.g., ifenprodil), and other glutamate antagonists [e.g., selfotel, 3-(2-carboxypiperazin-4-yl)propyl-1-phosphonic acid (CPP), D,L-(E)-2-amino-4-propyl-5-phosphono-3-pentenoic acid (CGP-39653)], up to doses that suppressed operant rates of responding. In contrast to other neg. modulators of the NMDA receptor studied, which typically decreased operant rates of responding at doses that lacked antinociceptive effects, perzinfotel did not modify response rates at doses that blocked irritant-induced thermal hypersensitivity. Collectively, these studies demonstrate that perzinfotel has therapeutic ratios for effectiveness vs. adverse effects superior to those seen with other competitive and uncompetitive NMDA receptor antagonists studied.

IT 144912-63-0, EAA-090

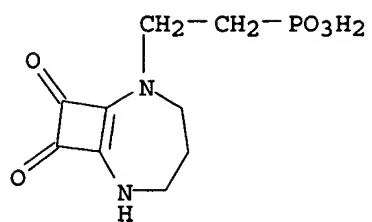
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(effects of N-Me-D-aspartate receptor antagonist perzinfotel [EAA-090] on chemical induced thermal hypersensitivity)

RN 144912-63-0 CAPLUS

CN Phosphonic acid, [2-(8,9-dioxo-2,6-diazabicyclo[5.2.0]non-1(7)-en-2-yl)ethyl]- (9CI) (CA INDEX NAME)

10/820,215



REFERENCE COUNT:

40

THERE ARE 40 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

10/820,215

see 3818
L2 ANSWER 4 OF 18 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2005:371071 CAPLUS
DOCUMENT NUMBER: 142:417206
TITLE: Oral administration of NMDA receptor antagonists
INVENTOR(S): Benjamin, Eric J.; Cloud, William F.; Ashraf,
Muhammad; Islam, Mohammed; Brandt, Michael R.;
Tremblay, Gerald F.
PATENT ASSIGNEE(S): Wyeth, John, and Brother Ltd., USA
SOURCE: PCT Int. Appl., 77 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 4
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---------------|--|----------|-----------------|----------|
| WO 2005037287 | A1 | 20050428 | WO 2004-US34113 | 20041014 |
| WO 2005037287 | C1 | 20050630 | | |
| W: | AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW | | | |
| RW: | BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | |

PRIORITY APPLN. INFO.: US 2003-511560P P 20031015

OTHER SOURCE(S): MARPAT 142:417206

AB Solid, oral pharmaceutical dosage forms of [2-(8,9-dioxo-2,6-diazabicyclo[5.2.0]non-1(7)-en-2-yl)alkyl]phosphonic acid and its derivs. (salts) as NMDA receptor antagonists are disclosed. In addition, methods of use are disclosed for the treatment, inter alia, of cerebral vascular disorders, anxiety disorders; mood disorders; schizophrenia; schizophreniform disorder; schizoaffective disorder; cognitive impairment; chronic neurodegenerative disorders; inflammatory diseases; fibromyalgia; complications from herpes zoster; prevention of tolerance to opiate analgesia; withdrawal symptoms from addictive drugs; and pain. For example, a capsule formulation was prepared by wet granulation comprising (i) an intragranular phase containing [2-[8,9-dioxo-2,6-diazabicyclo[5.2.0]non-1(7)-en-2-yl]ethyl]phosphonic acid 100 mg, Avicel PH 101 13.91 mg, povidone 3.61 mg, and croscarmellose sodium 5.77 mg, and (ii) an extragranular phase containing Avicel PH 101 14.42 mg, croscarmellose sodium 5.77 mg, and magnesium stearate 1.44 mg.

IT 144912-63-0

RL: PKT (Pharmacokinetics); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

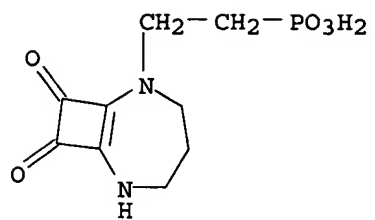
(preparation, bioavailability and therapeutic uses of oral compns. containing

phosphonate derivs. as NMDA antagonists)

RN 144912-63-0 CAPLUS

CN Phosphonic acid, [2-(8,9-dioxo-2,6-diazabicyclo[5.2.0]non-1(7)-en-2-yl)ethyl]- (9CI) (CA INDEX NAME)

10/820,215



REFERENCE COUNT:

2

THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

10/820,215

see 4917

L2 ANSWER 5 OF 18 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2005:371019 CAPLUS

DOCUMENT NUMBER: 142:411486

TITLE: Preparation of {2-[8,9-dioxo-2,6-diazabicyclo[5.2.0]non-1(7)-en-2-yl]ethyl}phosphonate esters by cyclocondensation reaction of squaric acid derivatives with (aminopropyl)aminoethanephosphonate esters and subsequent hydrolysis to free acid

INVENTOR(S): Wilk, Bogdan K.; Vid, Galina; Liu, Weiguo; Shi, Xinxu

PATENT ASSIGNEE(S): Wyeth, John, and Brother Ltd., USA

SOURCE: U.S. Pat. Appl. Publ., 10 pp.

CODEN: USXXCO

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---------------|------|----------|-----------------|----------|
| US 2005090470 | A1 | 20050428 | US 2004-969715 | 20041020 |
| WO 2005040176 | A2 | 20050506 | WO 2004-US34831 | 20041020 |
| WO 2005040176 | A3 | 20051201 | | |

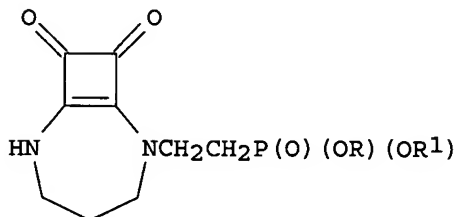
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RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

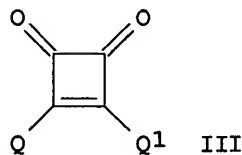
PRIORITY APPLN. INFO.: US 2003-513611P P 20031022

OTHER SOURCE(S): CASREACT 142:411486; MARPAT 142:411486

GI



I



III

AB {2-[8,9-Dioxo-2,6-diazabicyclo[5.2.0]non-1(7)-en-2-yl]ethyl}phosphonic acid (I; R = R₁ = H), useful as an NMDA antagonist appropriate for treatment of stroke, epilepsy, Alzheimer's and Parkinson's diseases and pain (no data), is prepared by hydrolysis of its esters I (R, R₁ = C₁-6 alkyl, C₁-6 haloalkyl; preferably R = R₁ = Et), which in turn are prepared by reaction of a 1,3-diaminopropane derivative H₂N(CH₂)₃NHCH₂CH₂P(O)(OR)(OR₁) (II; same R, R₁) with a cyclobutenedione (III; Q, Q₁ = OH, halo, OX₁; preferably Q, Q₁ = OEt or OH; X₁ = C₁-6 alkyl, C₁-6 haloalkyl, aryl) in a solvent HOX₁ (same X₁; preferably HOX₁ = MeOH or EtOH); compds. II are

prepared by reaction of 1,3-diaminopropane with $XCH_2CH_2P(O)(OR)(OR_1)$ or $CH_2:CHP(O)(OR)(OR_1)$ (same R, R_1 ; X = leaving group, preferably halo) at a ratio of $\geq 2:1$. In an example, treating 1.04 g di-Et squarate III ($Q = Q_1 = OEt$) in 250 mL MeOH with 1.46 g II ($R = R_1 = Et$; preparation given.) in 50 mL MeOH at 60° for 6 h and subsequent stirring overnight at room temperature gave 54% title ester I ($R = R_1 = Et$).

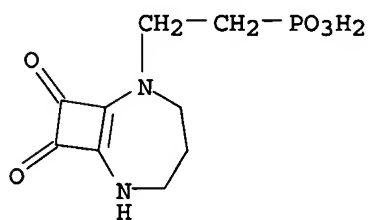
IT 144912-63-0P

RL: SPN (Synthetic preparation); PREP (Preparation)

(preparation of [[dioxodiazabicyclo[5.2.0]nonenyl]ethyl]phosphonates by cyclocondensation reaction of squaric acid derivs. with diaminopropane phosphonate derivs. and hydrolysis to give free acid)

RN 144912-63-0 CAPLUS

CN Phosphonic acid, [2-(8,9-dioxo-2,6-diazabicyclo[5.2.0]non-1(7)-en-2-yl)ethyl]- (9CI) (CA INDEX NAME)



10/820,215

~~10~~ ANSWER 6 OF 18 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2004:1059129 CAPLUS

DOCUMENT NUMBER: 142:32998

TITLE: Compositions of a cyclooxygenase-2 selective inhibitor and a cannabinoid agent for the treatment of central nervous system damage

INVENTOR(S): Stephenson, Diane T.; Taylor, Duncan P.

PATENT ASSIGNEE(S): Pharmacia Corporation, USA

SOURCE: PCT Int. Appl., 177 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---------------|------|----------|-----------------|----------|
| WO 2004105699 | A2 | 20041209 | WO 2004-US16496 | 20040526 |
| WO 2004105699 | A3 | 20051215 | | |

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2003-473820P P 20030528

OTHER SOURCE(S): MARPAT 142:32998

AB The present invention provides compns. and methods for the treatment of central nervous system damage in a subject. More particularly, the invention provides a combination therapy for the treatment of a central nervous system ischemic condition or a central nervous system traumatic injury comprising the administration to a subject of a cannabinoid agent in combination with a cyclooxygenase-2 selective inhibitor.

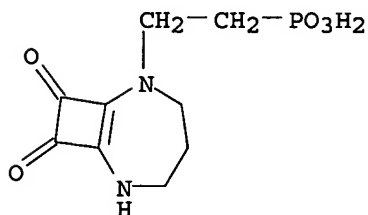
IT 144912-63-0

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(compns. of a cyclooxygenase-2 selective inhibitor and a cannabinoid agent for treatment of central nervous system damage)

RN 144912-63-0 CAPLUS

CN Phosphonic acid, [2-(8,9-dioxo-2,6-diazabicyclo[5.2.0]non-1(7)-en-2-yl)ethyl]- (9CI) (CA INDEX NAME)

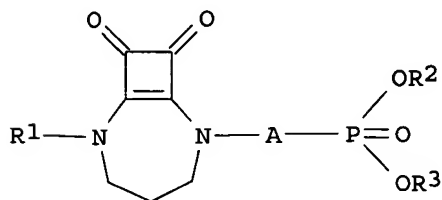


10/820,215

see 5017

L2 ANSWER 7 OF 18 CAPLUS COPYRIGHT 2006 ACS on STN
 ACCESSION NUMBER: 2004:902398 CAPLUS
 DOCUMENT NUMBER: 141:380023
 TITLE: Preparation of derivatives of 2-(8,9-dioxo-2,6-diazabicyclo(5.2.0)non-1(7)-en-2-yl)alkylphosphonic acid and their use as n-methyl-d-aspartate (nmda) receptor antagonists
 INVENTOR(S): Baudy, Reinhardt Bernhard; Butera, John Anthony
 PATENT ASSIGNEE(S): Wyeth, John, and Brother Ltd., USA
 SOURCE: PCT Int. Appl., 52 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 4
 PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|------|----------|--|------------|
| WO 2004092189 | A1 | 20041028 | WO 2004-US10596 | 20040407 |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW | | | | |
| RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |
| CA 2521313 | AA | 20041028 | CA 2004-2521313 | 20040407 |
| EP 1611144 | A1 | 20060104 | EP 2004-759168 | 20040407 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK, HR | | | | |
| PRIORITY APPLN. INFO.: | | | US 2003-461490P | P 20030409 |
| | | | WO 2004-US10596 | W 20040407 |
| OTHER SOURCE(S): | | | CASREACT 141:380023; MARPAT 141:380023 | |
| GI | | | | |



I

AB Preparation of title compds. I (at least one R2 or R3 is not hydrogen; R1 = H, C1-6 alkyl, C2-7 acyl, C1-6 alkanesulfonyl, C6-14 aroyl; R2, R3 = H, (un)substituted alkylcarboxyalkyl, alkoxycarboxyalkyl, aminocarboxyalkyl; A = C1-4 alkylene, C2-4 alkenylene) or pharmaceutically acceptable salts thereof are provided. The compds. of the present invention are N-methyl-D-aspartate (NMDA) receptor antagonists and are useful in

treating a variety of conditions present in a mammal that benefit from inhibiting the NMDA receptor. Thus, reaction of [2-(8,9-dioxo-2,6-diazabicyclo[5.2.0]non-1(7)-en-2-yl)ethyl]phosphonic acid with benzoic acid chloromethyl ester in DMF in the presence of N,N-diisopropylethylamine gave 99% title compound, 3-{2-[8,9-dioxo-2,6-diazabicyclo[5.2.0]non-1(7)-en-2-yl]ethyl}-3-oxido-7-oxo-7-phenyl-2,4,6-trioxa-3-phosphahept-1-yl benzoate.

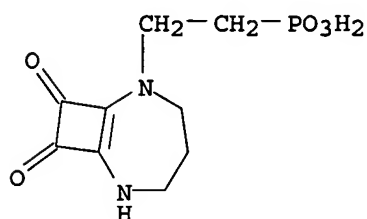
IT 144912-63-0

RL: RCT (Reactant); RACT (Reactant or reagent)

(preparation of derivs. of dioxodiazabicyclononenalkylphosphonic acid and their use as Me aspartate NMDA receptor antagonists)

RN 144912-63-0 CAPLUS

CN Phosphonic acid, [2-(8,9-dioxo-2,6-diazabicyclo[5.2.0]non-1(7)-en-2-yl)ethyl]- (9CI) (CA INDEX NAME)



REFERENCE COUNT:

22

THERE ARE 22 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

10/820,215

see 6017

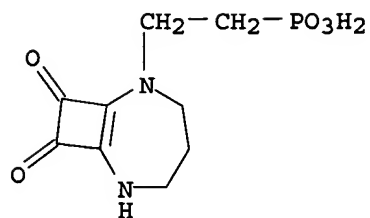
applicant

L2 ANSWER 8 OF 18 CAPLUS COPYRIGHT 2006 ACS on STN
 ACCESSION NUMBER: 2004:902198 CAPLUS
 DOCUMENT NUMBER: 141:370576
 TITLE: Intranasal pharmaceutical compositions containing
 [2-(8,9-dioxo-2,6-diazabicyclo[5.2.0]non-1(7)-en-2-yl)alkyl]phosphonic acid and its derivatives
 INVENTOR(S): Benjamin, Eric Joel; Baudy, Reinhardt Bernhard;
 Brandt, Michael Richard
 PATENT ASSIGNEE(S): Wyeth, John, and Brother Ltd., USA
 SOURCE: PCT Int. Appl., 46 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 4
 PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|------|----------|-----------------|------------|
| WO 2004091633 | A1 | 20041028 | WO 2004-US11668 | 20040407 |
| WO 2004091633 | C1 | 20050113 | | |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW | | | | |
| RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |
| CA 2521394 | AA | 20041028 | CA 2004-2521394 | 20040407 |
| EP 1622625 | A1 | 20060208 | EP 2004-759562 | 20040407 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK, HR | | | | |
| PRIORITY APPLN. INFO.: | | | US 2003-461571P | P 20030409 |
| | | | WO 2004-US11668 | W 20040407 |

OTHER SOURCE(S): MARPAT 141:370576
 AB Pharmaceutical compns. for intranasal administration contain the title compound or a salt thereof, and 1 or more additives for forming a composition for intranasal administration. Also provided are methods of treating conditions in a mammal associated with a glutamate abnormality that includes administering intranasally to a mammal a therapeutically effective amount of the above compds. Thus, a nasal solution contained [2-(8,9-dioxo-2,6-diazabicyclo[5.2.0]non-1(7)-en-2-yl)ethyl]phosphonic acid 30.0 and EDTA 0.10 g, 5N NaOH solution 37 and water 50 mL.
 IT 144912-63-0
 RL: PKT (Pharmacokinetics); RCT (Reactant); THU (Therapeutic use); BIOL (Biological study); RACT (Reactant or reagent); USES (Uses)
 (intranasal pharmaceutical compns. containing dioxo(diazabicyclononyl)alkylphosphonic acid and its derivs.)
 RN 144912-63-0 CAPLUS
 CN Phosphonic acid, [2-(8,9-dioxo-2,6-diazabicyclo[5.2.0]non-1(7)-en-2-yl)ethyl]- (9CI) (CA INDEX NAME)

10/820,215



REFERENCE COUNT:

4

THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

X ANSWER 9 OF 18 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2004:608723 CAPLUS

DOCUMENT NUMBER: 141:236333

TITLE: Characterization of two novel N-methyl-D-aspartate antagonists: EAA-090 (2-[8,9-dioxo-2,6-diazabicyclo[5.2.0]non-1(7)-en-2-yl]ethylphosphonic acid) and EAB-318 (R- α -amino-5-chloro-1-(phosphonomethyl)-1H-benzimidazole-2-propanoic acid hydrochloride)

AUTHOR(S): Sun, Lucy; Chiu, Doreen; Kowal, Dinne; Simon, Rachelle; Smeyne, Michelle; Zukin, R. Suzanne; Olney, John; Baudy, Reinhardt; Lin, Stephen

CORPORATE SOURCE: Discovery Neuroscience, Wyeth Research, Princeton, NJ, USA

SOURCE: Journal of Pharmacology and Experimental Therapeutics (2004), 310(2), 563-570

CODEN: JPETAB; ISSN: 0022-3565

PUBLISHER: American Society for Pharmacology and Experimental Therapeutics

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Two novel N-methyl-d-aspartate (NMDA) antagonists with unique chemical structures, EAA-090 (2-[8,9-dioxo-2,6-diazabicyclo[5.2.0]non-1(7)-en-2-yl]ethylphosphonic acid) and EAB-318 (R- α -amino-5-chloro-1-(phosphonomethyl)-1H-benzimidazole-2-propanoic acid hydrochloride), were compared with CGS-19755 (Selfotel) in ligand binding, electrophysiol., and neuroprotection assays. CGS-19755, EAA-090 and EAB-318 inhibited [3H]3-(2-carboxypiperazin-4-yl)propyl-1-phosphonic acid binding to NMDA receptors with IC50 values of 55, 28, and 7.9 nM, resp. All three compds. decreased the duration of spontaneous synaptic currents and inhibited NMDA-activated currents in rat hippocampal neurons. IC50 values for inhibition of current induced by 10 μ M NMDA were 795, 477, and 69 nM for CGS-19755, EAA-090, and EAB-318, resp. The NMDA antagonists protected chick embryo retina slices and cultured rat hippocampal and cortical neurons from glutamate- and NMDA-induced neurotoxicity. In expts. in which different NMDA receptor splice variants and subtypes were expressed in *Xenopus* oocytes, all three antagonists preferentially blocked NMDA-elicited currents mediated by N-methyl-d-aspartate receptor (NR)1 splice variants containing the N-terminal insertion. They also favored NR2A- vs. NR2B- or NR2C-containing NMDA receptors, with EAA-090 showing the greatest selectivity. EAA-090 was 10 times more potent at blocking NR2A- vs. NR2B- or NR2C-containing NMDA receptors. In addition to being the most potent NMDA antagonist, EAB-318 inhibited α -amino-3-hydroxy-5-methyl-4-isoxazole propionic acid (AMPA) and kainate receptors. The combination of NMDA and AMPA/kainate block enabled EAB-318 to protect neurons against ischemia induced cell death.

IT 144912-63-0, EAA-090

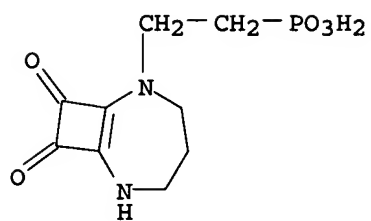
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(two novel N-Me-D-aspartate antagonists, EAA-090 and EAB-318)

RN 144912-63-0 CAPLUS

CN Phosphonic acid, [2-(8,9-dioxo-2,6-diazabicyclo[5.2.0]non-1(7)-en-2-yl)ethyl]- (9CI) (CA INDEX NAME)

10/820,215



REFERENCE COUNT:

34

THERE ARE 34 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

10/820,215

ANSWER 10 OF 18 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2004:353140 CAPLUS
DOCUMENT NUMBER: 140:380634
TITLE: Compositions of cyclooxygenase-2 selective inhibitors and NMDA receptor antagonists for the treatment or prevention of neuropathic pain
INVENTOR(S): Cheung, Raymond Y.
PATENT ASSIGNEE(S): Pharmacia Corporation, USA
SOURCE: U.S. Pat. Appl. Publ., 51 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---------------|------|----------|-----------------|----------|
| US 2004082543 | A1 | 20040429 | US 2002-282660 | 20021029 |
| WO 2004039371 | A2 | 20040513 | WO 2003-US33089 | 20031017 |
| WO 2004039371 | A3 | 20040617 | | |

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2002-282660 A 20021029

OTHER SOURCE(S): MARPAT 140:380634

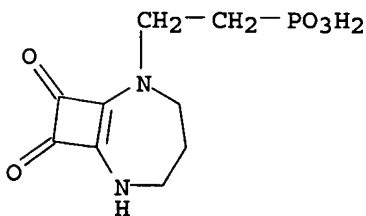
AB The present invention provides compns. and methods to treat or prevent neuropathic pain in a subject using a combination of a COX-2 selective inhibitor and a NMDA receptor antagonist.

IT 144912-63-0

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(compns. of cyclooxygenase-2 selective inhibitors and NMDA receptor antagonists for treatment or prevention of neuropathic pain)

RN 144912-63-0 CAPLUS

CN Phosphonic acid, [2-(8,9-dioxo-2,6-diazabicyclo[5.2.0]non-1(7)-en-2-yl)ethyl]- (9CI) (CA INDEX NAME)



10/820,215

see 7 & 17

L2 ANSWER 11 OF 18 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2003:301059 CAPLUS

DOCUMENT NUMBER: 138:314606

TITLE: [[2-(amino-3,4-dioxo-1-cyclobuten-1-yl)amino]alkyl]-
acid derivatives for the treatment of pain

INVENTOR(S): Brandt, Michael Richard; Zaleska, Margaret Maria;
Moyer, John Allen

PATENT ASSIGNEE(S): Wyeth, John, and Brother Ltd., USA

SOURCE: PCT Int. Appl., 40 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

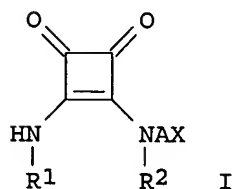
FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|------|----------|-----------------|------------|
| WO 2003031416 | A2 | 20030417 | WO 2002-US32252 | 20021009 |
| WO 2003031416 | A3 | 20030814 | | |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW | | | | |
| RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |
| CA 2461348 | AA | 20030417 | CA 2002-2461348 | 20021009 |
| US 2003114444 | A1 | 20030619 | US 2002-267159 | 20021009 |
| EP 1434588 | A2 | 20040707 | EP 2002-789180 | 20021009 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK | | | | |
| BR 2002013237 | A | 20040928 | BR 2002-13237 | 20021009 |
| JP 2005508950 | T2 | 20050407 | JP 2003-534400 | 20021009 |
| NO 2004001378 | A | 20040528 | NO 2004-1378 | 20040402 |
| PRIORITY APPLN. INFO.: | | | US 2001-328245P | P 20011010 |
| | | | WO 2002-US32252 | W 20021009 |

OTHER SOURCE(S): MARPAT 138:314606

GI



AB The invention provides a method for treating pain in a mammal that includes administering I [R1 = H, C1-6 alkyl, C7-12 phenylalkyl; R2 = H, C1-6 alkyl, C2-6 alkenyl, C7-12 phenylalkyl; or R1 and R2 taken together as Z are CH2CH2, CH2C(R6)(R7)CH2, CH2C(R8)(R9)C(R10)(R11)CH2; R6, R8, R10 = H, C1-6 alkyl, OH; R7, R9, R11 = H, C1-6 alkyl; A = C1-6 alkylene, C2-6

10/820,215

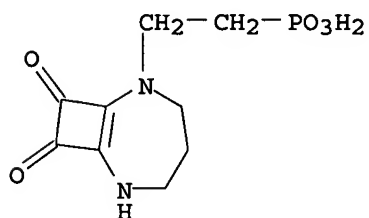
alkenylene; X = CO₂R₃, P(O)(OR₄)(OR₅), 3,5-dioxo-1,2,4-oxadiazolidin-2-yl, 5-tetrazolyl; R₃, R₄, R₅ = H, C1-6 alkyl], or a pharmaceutically acceptable salt thereof. Also provided are compns. for treating pain containing I.

IT 144912-63-0

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(aminodioxocyclobutenyl derivs. for treatment of pain)

RN 144912-63-0 CAPLUS

CN Phosphonic acid, [2-(8,9-dioxo-2,6-diazabicyclo[5.2.0]non-1(7)-en-2-yl)ethyl]- (9CI) (CA INDEX NAME)



L2 ANSWER 12 OF 18 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2002:863891 CAPLUS
DOCUMENT NUMBER: 139:16866
TITLE: EAA-090: Neuroprotectant competitive NMDA antagonist
AUTHOR(S): Childers, Wayne E., Jr.; Abou-Gharbia, Magid A.;
Moyer, John A.; Zaleska, Margaret M.
CORPORATE SOURCE: Chemical Sciences, Wyeth Research, Princeton, NJ,
08543-8000, USA
SOURCE: Drugs of the Future (2002), 27(7), 633-638
CODEN: DRFUD4; ISSN: 0377-8282
PUBLISHER: Prous Science
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

AB A review. EAA-090 is a novel squaric acid amide derivative that has been identified as a potential treatment for the ischemic brain damage resulting from stroke. EAA-090 is a competitive inhibitor at the NMDA-selective subtype of the glutamate receptor. The compound demonstrates potent inhibitory activity in both in vitro and in vivo models of NMDA-induced excitotoxicity and provides neuroprotective efficacy in several animal models of stroke. EAA-090 is unique among competitive NMDA antagonists in displaying a clear separation between predicted efficacious dose and doses that induce PCP-like psychotomimetic side effects in both animals and humans. This unique profile makes EAA-090 an exciting candidate for assessing the neuroprotective potential of the competitive NMDA mechanism.

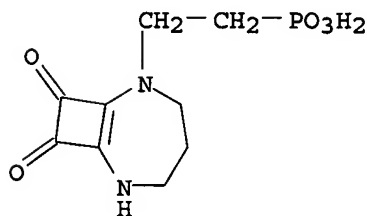
IT 144912-63-0, EAA 090

RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(Way 126090; neuroprotectant NMDA antagonist EAA-090 for ischemic brain damage resulting from stroke)

RN 144912-63-0 CAPLUS

CN Phosphonic acid, [2-(8,9-dioxo-2,6-diazabicyclo[5.2.0]non-1(7)-en-2-yl)ethyl]- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 26 THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 13 OF 18 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2001:260977 CAPLUS

DOCUMENT NUMBER: 135:61386

TITLE: Design, Synthesis, SAR, and Biological Evaluation of
Highly Potent Benzimidazole-Spaced
Phosphono- α -Amino Acid Competitive NMDA
Antagonists of the AP-6 TypeAUTHOR(S): Baudy, Reinhardt B.; Fletcher, Horace, III; Yardley,
John P.; Zaleska, Margaret M.; Bramlett, Donna R.;
Tasse, Rene P.; Kowal, Dianne M.; Katz, Alan H.;
Moyer, John A.; Abou-Gharbia, MagidCORPORATE SOURCE: Chemical Sciences and Division of Neuroscience,
Wyeth-Ayerst Research, Princeton, NJ, 08543-8000, USASOURCE: Journal of Medicinal Chemistry (2001), 44(10),
1516-1529

CODEN: JMCMAR; ISSN: 0022-2623

PUBLISHER: American Chemical Society

DOCUMENT TYPE: Journal

LANGUAGE: English

OTHER SOURCE(S): CASREACT 135:61386

AB 2-Amino-(phosphonoalkyl)-1H-benzimidazole-2-alkanoic acids were synthesized and evaluated for NMDA receptor affinity using a [3H]CPP binding assay. Functional antagonism of the NMDA receptor complex was evaluated in vitro using a stimulated [3H]TCP binding assay and in vivo by employing an NMDA-induced seizure model. Several compds. of the AP-6 type demonstrated potent and selective NMDA antagonistic activity both in vitro and in vivo. In particular, [R(-)]-2-amino-3-(5-chloro-1-phosphonomethyl-1H-benzimidazol-2-yl)propionic acid (1) displayed an IC₅₀ value of 7.1 nM in the [3H]CPP binding assay and an ED₅₀ value of 0.13 mg/kg (i.p.) in the NMDA lethality model. Compound 1, when administered i.v. as a single bolus dose of 3 mg/kg following permanent occlusion of the middle cerebral artery in the rat, reduced the volume of infarcted brain tissue by 45%. These results support a promising therapeutic potential for compound 1 as a neuroprotective agent.

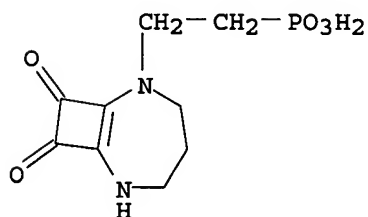
IT 144912-63-0, EAA 090

RL: PRP (Properties)

(comparison of conformation of benzimidazole-spaced
phosphono- α -amino acid competitive NMDA antagonist to that of)

RN 144912-63-0 CAPLUS

CN Phosphonic acid, [2-(8,9-dioxo-2,6-diazabicyclo[5.2.0]non-1(7)-en-2-yl)ethyl]- (9CI) (CA INDEX NAME)



REFERENCE COUNT:

37

THERE ARE 37 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

10/820,215

see 8 of 17

12 ANSWER 14 OF 18 CAPLUS COPYRIGHT 2006 ACS on STN
 ACCESSION NUMBER: 1999:748347 CAPLUS
 DOCUMENT NUMBER: 131:337040
 TITLE: Preparation of [2-(8,9-dioxo-2,6-diazabicyclo[5.2.0]non-1(7)-en-2-yl)ethyl]phosphonic acid
 INVENTOR(S): Asselin, Andre A.; Kinney, William A.; Schmid, Jean
 PATENT ASSIGNEE(S): American Home Products Corporation, USA
 SOURCE: U.S., 6 pp.
 CODEN: USXXAM
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------------------------|------|----------|-----------------|-------------|
| US 5990307 | A | 19991123 | US 1998-127202 | 19980731 |
| US 6011168 | A | 20000104 | US 1999-375345 | 19990816 |
| PRIORITY APPLN. INFO.: | | | US 1997-54553P | P 19970801 |
| | | | US 1998-127202 | A3 19980731 |

OTHER SOURCE(S): CASREACT 131:337040

AB [2-(8,9-Dioxo-2,6-diazabicyclo[5.2.0]non-1(7)-en-2-yl)ethyl]phosphonic acid (I) was prepared by reaction of Me₃CO₂CNH(CH₂)₃NH₂ with a dialkyl vinylphosphonate to obtain N-[3-(t-butyloxycarbonylamino)propyl]-2-aminoethylphosphonic acid dialkyl ester in 80% yield. Reaction of the latter with a 3,4-dialkoxycyclobut-3-en-1,2-dione gave [3-[[2-(dialkoxyphosphoryl)ethyl]-(2-alkoxy-3,4-dioxo-1,2-cyclobuten-1-yl)amino]propyl]carbamic acid 1,1-dimethylethyl ester in 96% yield. Deprotection and cyclization of this in CF₃CO₂H gave [2-((8,9)-dioxo-2,6-diazabicyclo[5.2.0]-non-1(7)-en-2-yl)ethyl]phosphonic acid dialkyl ester in 58% yield; treatment with BrSiMe₃ gave I in 38.8% overall yield.

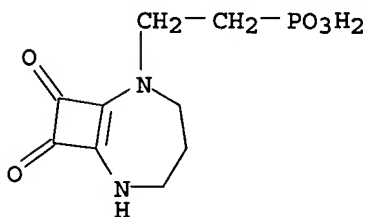
IT 144912-63-0P

RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)

(preparation of [2-(8,9-dioxo-2,6-diazabicyclo[5.2.0]non-1(7)-en-2-yl)ethyl]phosphonic acid)

RN 144912-63-0 CAPLUS

CN Phosphonic acid, [2-(8,9-dioxo-2,6-diazabicyclo[5.2.0]non-1(7)-en-2-yl)ethyl]- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 15 OF 18 CAPLUS COPYRIGHT 2006 ACS on STN

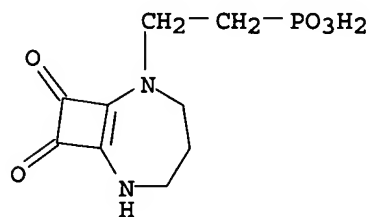
ACCESSION NUMBER: 1999:113692 CAPLUS
 DOCUMENT NUMBER: 130:153793
 TITLE: Preparation of [2-(8,9-dioxo-2,6-diazabicyclo[5.2.0]non-1(7)-en-2-yl)ethyl]phosphonic acid
 INVENTOR(S): Asselin, Andre Alfred; Kinney, William Alvin; Schmid, Jean
 PATENT ASSIGNEE(S): American Home Products Corporation, USA
 SOURCE: PCT Int. Appl., 17 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|--|------|----------|------------------|------------|
| WO 9906417 | A1 | 19990211 | WO 1998-US15841 | 19980731 |
| W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG | | | | |
| CA 2297411 | AA | 19990211 | CA 1998-2297411 | 19980731 |
| AU 9886037 | A1 | 19990222 | AU 1998-86037 | 19980731 |
| AU 746119 | B2 | 20020418 | | |
| EP 1000072 | A1 | 20000517 | EP 1998-937292 | 19980731 |
| EP 1000072 | B1 | 20030219 | | |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, SI, LT, LV, FI, RO | | | | |
| BR 9811807 | A | 20000815 | BR 1998-11807 | 19980731 |
| JP 2001512129 | T2 | 20010821 | JP 2000-505174 | 19980731 |
| NZ 502509 | A | 20020828 | NZ 1998-502509 | 19980731 |
| AT 232875 | E | 20030315 | AT 1998-937292 | 19980731 |
| RU 2205834 | C2 | 20030610 | RU 2000-105273 | 19980731 |
| ES 2190091 | T3 | 20030716 | ES 1998-937292 | 19980731 |
| CN 1526714 | A | 20040908 | CN 2003-10120120 | 19980731 |
| NO 2000000488 | A | 20000131 | NO 2000-488 | 20000131 |
| HK 1027814 | A1 | 20030516 | HK 2000-107097 | 20001108 |
| PRIORITY APPLN. INFO.: | | | US 1997-905091 | A 19970801 |
| | | | WO 1998-US15841 | W 19980731 |
| AB The title compound (I), an NMDA antagonist, was useful as an anticonvulsant and neuroprotectant in situations involving excess release of excitatory amino acids. 3-Aminopropylcarbamic acid 1,1-dimethyl-Et ester was treated with a dialkyl vinylphosphonate (alkyl = Me, Et) to obtain N-[3-(tert-butyloxycarbonylamino)propyl]-2-aminoethylphosphonic acid dialkyl ester (II) in 80% yield. Reaction of II with 3,4-diethoxycyclobut-3-ene-1,2-dione gave [3-[[2-(dialkoxyphosphoryl)ethyl]-(2-alkoxy-3,4-dioxo-1,2-cyclobuten-1-yl)amino]propyl]carbamic acid 1,1-dimethylethyl ester (III) in 96% yield. Deprotection and cyclization of III in HO2CCF3 gives [2-(8,9-dioxo-2,6-diazabicyclo[5.2.0]non-1(7)-en-2-yl)ethyl]phosphonic acid dialkyl ester (IV) in 58% yield. Compound IV was treated with bromotrimethylsilane to give I. | | | | |
| IT 144912-63-0P RL: SPN (Synthetic preparation); PREP (Preparation) (preparation of) | | | | |

10/820,215

RN 144912-63-0 CAPLUS

CN Phosphonic acid, [2-(8,9-dioxo-2,6-diazabicyclo[5.2.0]non-1(7)-en-2-yl)ethyl]- (9CI) (CA INDEX NAME)



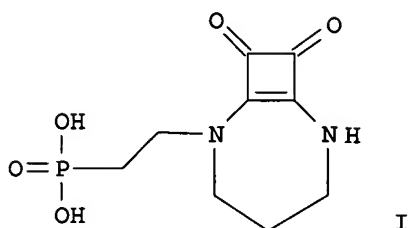
REFERENCE COUNT:

1

THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 16 OF 18 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1998:9157 CAPLUS
 DOCUMENT NUMBER: 128:75452
 TITLE: Design and Synthesis of [2-(8,9-Dioxo-2,6-diazabicyclo[5.2.0]non-1(7)-en-2-yl)ethyl]phosphonic Acid (EAA-090), a Potent N-Methyl-D-aspartate Antagonist, via the Use of 3-Cyclobutene-1,2-dione as an Achiral α -Amino Acid Bioisostere
 AUTHOR(S): Kinney, William A.; Abou-Gharbia, Magid; Garrison, Deanna T.; Schmid, Jean; Kowal, Dianne M.; Bramlett, Donna R.; Miller, Tracy L.; Tasse, Rene P.; Zaleska, Margaret M.; Moyer, John A.
 CORPORATE SOURCE: Chemical Sciences CNS Disorders Divisions, Wyeth-Ayerst Research, Princeton, NJ, 08543-8000, USA
 SOURCE: Journal of Medicinal Chemistry (1998), 41(2), 236-246
 CODEN: JMCMAR; ISSN: 0022-2623
 PUBLISHER: American Chemical Society
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 OTHER SOURCE(S): CASREACT 128:75452
 GI



AB The diazabicyclic amino acid phosphonate I, [2-(8,9-dioxo-2,6-diazabicyclo[5.2.0]non-1(7)-en-2-yl)ethyl]phosphonic acid, was identified as a potent NMDA antagonist. It contains the α -amino acid bioisostere 3,4-diamino-3-cyclobutene-1,2-dione and an addnl. ring for conformational rigidity. I was as potent as CGS-19755 in the [3H]CPP binding assay, the stimulated [3H]TCP binding assay, and the NMDA-induced lethality model in mice. A single bolus dose of I, administered i.v. following permanent occlusion of middle cerebral artery (MCA) in the rat, reduced the size of infarcted tissue by 57%. Structure-activity relationship (SAR) studies have indicated that the six- and eight-membered ring derivs. had diminished activity and that the two-carbon side chain length was optimum for NMDA receptor affinity. Substitution on the ring was counterproductive in the case of sterically demanding di-Me groups and of no consequence in the case of an H-bonding hydroxyl group. Replacement of the phosphonic acid group by either a carboxylic acid or a tetrazole group was unproductive. The potent bicyclic NMDA antagonists were synthesized efficiently by virtue of their achiral nature and the ease of vinyllogous amide formation from squaric acid esters. I, being a unique NMDA antagonist structural type with a favorable preclin. profile, may offer advantages over existing NMDA antagonists for the treatment of neurol. disorders such as stroke and head trauma. I is currently under clin. evaluation as a neuroprotective agent for stroke.

IT 144912-63-0P

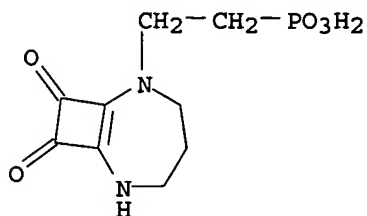
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

10/820,215

(design and synthesis of [(dioxodiazabicyclononyl)ethyl]phosphonic acid as a potent NMDA antagonist via use of cyclobutenedione as achiral amino acid bioisostere)

RN 144912-63-0 CAPLUS

CN Phosphonic acid, [2-(8,9-dioxo-2,6-diazabicyclo[5.2.0]non-1(7)-en-2-yl)ethyl]- (9CI) (CA INDEX NAME)



REFERENCE COUNT:

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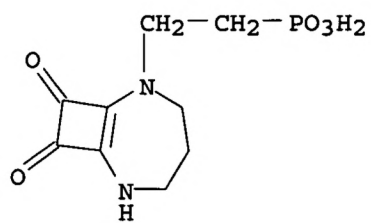
THERE ARE 38 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 17 OF 18 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1997:480831 CAPLUS
 DOCUMENT NUMBER: 127:90514
 TITLE: Rapamycin-derived neuroprotective agents
 INVENTOR(S): Lin, Stephen Shi-Hsun; Molnar-Kimber, Katherine Lu
 PATENT ASSIGNEE(S): American Home Products Corporation, USA; Wyeth
 SOURCE: Eur. Pat. Appl., 11 pp.
 CODEN: EPXXDW
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|--|----------|------------------|------------|
| EP 778023 | A1 | 19970611 | EP 1996-308786 | 19961204 |
| EP 778023 | B1 | 20030312 | | |
| R: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE | | | | |
| TW 427904 | B | 20010401 | TW 1996-85114700 | 19961128 |
| AT 234095 | E | 20030315 | AT 1996-308786 | 19961204 |
| ES 2188730 | T3 | 20030701 | ES 1996-308786 | 19961204 |
| AU 9674178 | A1 | 19970612 | AU 1996-74178 | 19961205 |
| AU 700653 | B2 | 19990114 | | |
| ZA 9610245 | A | 19980605 | ZA 1996-10245 | 19961205 |
| NZ 299888 | A | 20010223 | NZ 1996-299888 | 19961205 |
| CA 2192298 | AA | 19970608 | CA 1996-2192298 | 19961206 |
| NO 9605238 | A | 19970609 | NO 1996-5238 | 19961206 |
| NO 309966 | B1 | 20010430 | | |
| JP 09183727 | A2 | 19970715 | JP 1996-326582 | 19961206 |
| CN 1159915 | A | 19970924 | CN 1996-123098 | 19961206 |
| CN 1112925 | B | 20030702 | | |
| BR 9605895 | A | 19980818 | BR 1996-5895 | 19961206 |
| IL 119778 | A1 | 19990714 | IL 1996-119778 | 19961206 |
| HK 1009938 | A1 | 20030627 | HK 1998-110870 | 19980923 |
| PRIORITY APPLN. INFO.: | | | US 1995-8337P | P 19951207 |
| AB | Rapamycin, rapamycin 1,3-Diels-Alder adducts with phenyltriazolinedione or methyltriazolinedione, rapamycin 42-ester with 4-[[4-(dimethylamino)phenyl]azo]benzenesulfonic acid, and rapamycin O-benzyl-27-oxime are useful as neuroprotective agents in treatment of stroke, head trauma, or neurodegenerative disorders such as Alzheimer's disease, amyotrophic lateral sclerosis, epilepsy, Huntington's disease, and parkinsonism. These compds. may be used in combination with NMDA or AMPA antagonists. Thus, rapamycin (200 nM) protected rat hippocampal and cortical cells against glutamate (30 µM) toxicity. | | | |
| IT | 144912-63-0 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses) (enhancement of action of; rapamycin-derived neuroprotective agents) | | | |
| RN | 144912-63-0 CAPLUS | | | |
| CN | Phosphonic acid, [2-(8,9-dioxo-2,6-diazabicyclo[5.2.0]non-1(7)-en-2-yl)ethyl]- (9CI) (CA INDEX NAME) | | | |

10/820,215



12817

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|------|----------|-----------------|------------|
| EP 496561 | A2 | 19920729 | EP 1992-300472 | 19920120 |
| EP 496561 | A3 | 19921223 | | |
| EP 496561 | B1 | 19950315 | | |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, PT, SE | | | | |
| US 5168103 | A | 19921201 | US 1991-806861 | 19911217 |
| IL 100679 | A1 | 19961031 | IL 1992-100679 | 19920116 |
| AU 9210301 | A1 | 19920730 | AU 1992-10301 | 19920117 |
| AU 639629 | B2 | 19930729 | | |
| ZA 9200358 | A | 19930719 | ZA 1992-358 | 19920117 |
| SK 280268 | B6 | 19991008 | SK 1992-144 | 19920117 |
| CZ 286407 | B6 | 20000412 | CZ 1992-144 | 19920117 |
| CA 2059704 | AA | 19920723 | CA 1992-2059704 | 19920120 |
| CA 2059704 | C | 20020716 | | |
| JP 04321654 | A2 | 19921111 | JP 1992-7385 | 19920120 |
| JP 3167770 | B2 | 20010521 | | |
| AT 119873 | E | 19950415 | AT 1992-300472 | 19920120 |
| ES 2071428 | T3 | 19950616 | ES 1992-300472 | 19920120 |
| RU 2039035 | C1 | 19950709 | RU 1992-5010645 | 19920120 |
| FI 9200261 | A | 19920823 | FI 1992-261 | 19920121 |
| FI 105551 | B1 | 20000915 | | |
| HU 61970 | A2 | 19930329 | HU 1992-192 | 19920121 |
| HU 215838 | B | 20000628 | | |
| KR 206055 | B1 | 19990701 | KR 1992-780 | 19920121 |
| US 5240946 | A | 19930831 | US 1992-875925 | 19920429 |
| PRIORITY APPLN. INFO.: | | | | |
| | | | US 1991-644157 | A 19910122 |
| | | | US 1991-806861 | A 19911217 |
| | | | CS 1992-144 | A 19920117 |

O=C1C(=O)C(R1N)C(R2AX)C1

Page 31

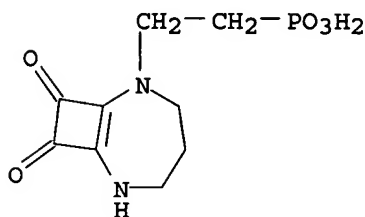
R9, R11 = H, alkyl; A = alkylene, alkenylene; X = CO₂R₃, P(O)(OR₄)OR₅, 3,5-dioxo-1,2,4-oxazolidin-2-yl, 5-tetrazolyl; R₃, R₄, R₅ = H, alkyl], were prepared. Thus, H₂NCH₂CH(OH)CH₂NH₂ was treated with O(CO₂CMe₃)₂ in MeCN to give H₂NCH₂CH(OH)CH₂NHCO₂CMe₃. The latter was condensed with BrCH₂CH₂P(O)(OEt)₂ using Na₂CO₃ in EtOH to give (EtO)₂P(O)CH₂CH₂NHCH₂CH(OH)CH₂NHCO₂CMe₃. This was condensed with 3,4-diethoxy-3-cyclobutene-1,2-dione in EtOH to give 3-[N-[2-(diethoxyphosphinyl)ethyl]-N-(2-ethoxy-3,4-dioxo-1-cyclobuten-1-yl)amino]-2-hydroxypropyl]carbamic acid 1,1-dimethylethyl ester. This was stirred with HCO₂H and the residue was refluxed with EtN(CHMe₂)₂ in EtOH to give [2-(4-hydroxy-8,9-dioxo-2,6-diazabicyclo[5.2.0]non-1(7)-en-2-yl)ethyl]phosphonic acid di-Et ester. This was refluxed with Me₃SiBr in ClCH₂CH₂Cl to give [2-(4-hydroxy-8,9-dioxo-2,6-diazabicyclo[5.2.0]non-1(7)-en-2-yl)ethyl]phosphonic acid. The latter inhibited N-methyl-D-aspartate-induced lethality in mice with ED₅₀ = 1.8 ng/kg.

IT **144912-63-0P**

RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of, as NMDA antagonist)

RN 144912-63-0 CAPLUS

CN Phosphonic acid, [2-(8,9-dioxo-2,6-diazabicyclo[5.2.0]non-1(7)-en-2-yl)ethyl]- (9CI) (CA INDEX NAME)



10/820,215

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FILE 'REGISTRY' ENTERED AT 15:53:05 ON 15 FEB 2006

L1 STRUCTURE UPLOADED

L2 2 S L1

L3 39 S L1 SSS FUL

FILE 'CAPLUS' ENTERED AT 15:53:53 ON 15 FEB 2006

L4 25 S L3

L5 ANALYZE L4 1- RN HIT : 39 TERMS

FILE 'REGISTRY' ENTERED AT 15:54:07 ON 15 FEB 2006

L6 1 S 144912-63-0/RN

L7 38 S L3 NOT L6

FILE 'CAPLUS' ENTERED AT 15:56:04 ON 15 FEB 2006

L8 17 S L7

L9 18 S L6

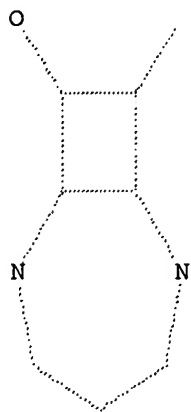
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L11 17 S L8 OR L10

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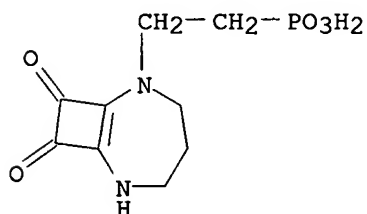
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10/820,215

L6 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2006 ACS on STN
RN **144912-63-0** REGISTRY
ED Entered STN: 15 Dec 1992
CN Phosphonic acid, [2-(8,9-dioxo-2,6-diazabicyclo[5.2.0]non-1(7)-en-2-yl)ethyl]- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN 2,6-Diazabicyclo[5.2.0]nonane, phosphonic acid deriv.
OTHER NAMES:
CN EAA 090
CN Perzinfotel
CN Way 126090
FS 3D CONCORD
MF C9 H13 N2 O5 P
CI COM
SR CA
LC STN Files: ADISINSIGHT, BIOSIS, CA, CAPLUS, CASREACT, IMSDRUGNEWS, IMSRESEARCH, IPA, PHAR, PROMT, PROUSDDR, SYNTHLINE, TOXCENTER, USAN, USPATFULL



****PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT****

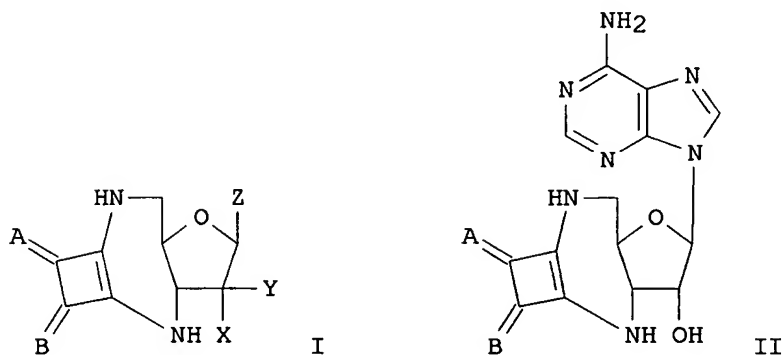
18 REFERENCES IN FILE CA (1907 TO DATE)
18 REFERENCES IN FILE CAPLUS (1907 TO DATE)

10/820,215

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~~LV~~ ANSWER 1 OF 17 CAPLUS COPYRIGHT 2006 ACS on STN
 ACCESSION NUMBER: 2005:1003147 CAPLUS
 DOCUMENT NUMBER: 143:286635
 TITLE: Preparation of 3',5'-N,N'-(3,4-dioxocyclobutene-1,2-diyl)-3',5'-diamino-3',5'-dideoxynucleoside derivative as cyclic nucleotide analog
 INVENTOR(S): Sekine, Mitsuo; Seio, Yasushi; Miyashita, Takuhei
 PATENT ASSIGNEE(S): Japan Science and Technology Agency, Japan
 SOURCE: Jpn. Kokai Tokkyo Koho, 5 pp.
 CODEN: JKXXAF
 DOCUMENT TYPE: Patent
 LANGUAGE: Japanese
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------------------------|--|----------|-----------------|----------|
| JP 2005247772 | A2 | 20050915 | JP 2004-61638 | 20040305 |
| PRIORITY APPLN. INFO.: | | | JP 2004-61638 | 20040305 |
| OTHER SOURCE(S): | CASREACT 143:286635; MARPAT 143:286635 | | | |
| GI | | | | |



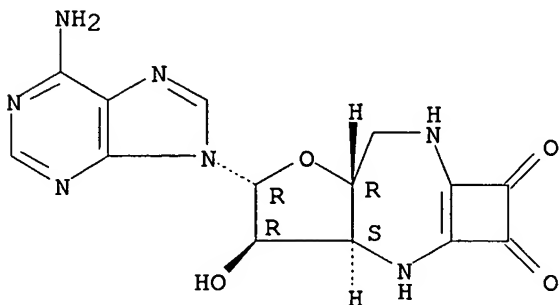
AB A 3',5'-diamino-3',5'-dideoxy-nucleoside derivative having squaric acid diamide skeleton (I) [A, B = O, S; one of X and Y = H and the other = H, halo, OH, NH₂, alkylamino, dialkylamino, alkoxy, alkoxyalkyl, aryloxyalkyl, arylthio, alkylthio, cyano, acylamino; Z = (un)substituted purin or pyrimidine base] is prepared This compound is relatively stable in vivo and exhibits resistance against degrading enzymes and is useful as an inhibitor or activator of intracellular or extracellular signal transduction (no data). Thus, 48 mg 3',5'-diamino-3',5'-dideoxyadenosine was dissolved in 1.5 mL MeOH, treated with 12.8 μ L N,N-diisopropylethylamine and 17.1 mg 1,2-dimethoxy-3,4-dioxocyclobutene, and stirred at room temperature for 23 h to give, after purification by C-18 chromatog., 10 mg 3',5'-N,N'-(3,4-dioxocyclobutene-1,2-diyl)--3',5'-diamino-3',5'-dideoxyadenosine (II).
 IT **864248-74-8P**
 RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of 3',5'-N,N'-(3,4-dioxocyclobutene-1,2-diyl)-3',5'-diamino-3',5'-dideoxy-nucleoside derivative as cyclic nucleotide analog and cellular signal transduction activator or inhibitor)

RN 864248-74-8 CAPLUS

CN 2H-Cyclobuta[b]furo[3,2-e][1,4]diazepine-5,6-dione, 2-(6-amino-9H-purin-9-yl)-3,3a,4,7,8,8a-hexahydro-3-hydroxy-, (2R,3R,3aS,8aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L11 ANSWER 2 OF 17 CAPLUS COPYRIGHT 2006 ACS on STN
 ACCESSION NUMBER: 2005:572349 CAPLUS
 DOCUMENT NUMBER: 143:103227
 TITLE: Oral administration of [2-(8,9-dioxo-2,6-diazabicyclo[5.2.0]non-1(7)-en-2-yl)alkyl] phosphonic acid and derivatives
 INVENTOR(S): Benjamin, Eric J.; Cloud, William F.; Ashraf, Muhammad; Islam, Mohammed; Brandt, Michael R.; Tremblay, Gerald F.
 PATENT ASSIGNEE(S): Wyeth, John, and Brother Ltd., USA
 SOURCE: U.S. Pat. Appl. Publ., 32 pp.
 CODEN: USXXCO
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 4
 PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------------------------|------|----------|-----------------|------------|
| US 2005142192 | A1 | 20050630 | US 2004-961871 | 20041008 |
| US 2005004079 | A1 | 20050106 | US 2004-820215 | 20040407 |
| US 2005004080 | A1 | 20050106 | US 2004-820216 | 20040407 |
| PRIORITY APPLN. INFO.: | | | US 2003-511560P | P 20031015 |
| | | | US 2004-820215 | A 20040407 |
| | | | US 2004-820216 | A 20040407 |
| | | | US 2003-461490P | P 20030409 |
| | | | US 2003-461571P | P 20030409 |

OTHER SOURCE(S): MARPAT 143:103227

AB Solid, pharmaceutical dosage forms of [2-(8,9-dioxo-2,6-diazabicyclo[5.2.0]non-1(7)-en-2-yl)alkyl]phosphonic acid and derivs. thereof are disclosed. In addition, methods of use are disclosed for the treatment, inter alia, of cerebral vascular disorders, anxiety disorders; mood disorders; schizophrenia; schizophreniform disorder; schizoaffective disorder; cognitive impairment; chronic neurodegenerative disorders; inflammatory diseases; fibromyalgia; complications from herpes zoster; prevention of tolerance to opiate analgesia; withdrawal symptoms from addictive drugs; and pain. For example, enteric coated tablets contained [2-(8,9-dioxo-2,6-diazabicyclo[5.2.0]non-1(7)-en-2-yl)ethyl] phosphonic acid 200, croscarmellose sodium 7.05, Povidone 3.53, Avicel PH101 14.1, croscarmellose sodium 4.7, sodium lauryl sulfate 5.88 and magnesium stearate 1.18 mg.

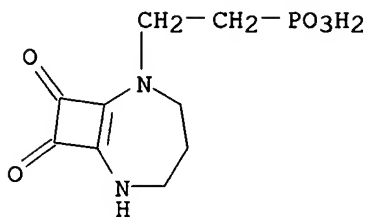
IT 144912-63-0 780765-59-5 780765-64-2
 780765-66-4 780765-67-5 782452-07-7
 782452-08-8 782452-09-9 782452-10-2
 782452-11-3

RL: PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(oral administration of [2-(8,9-dioxo-2,6-diazabicyclo[5.2.0]non-1(7)-en-2-yl)alkyl] phosphonic acid and derivs. for the treatment of mental disorders and inflammatory diseases and pain relief)

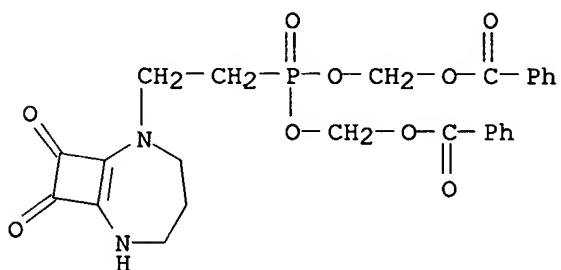
RN 144912-63-0 CAPLUS

CN Phosphonic acid, [2-(8,9-dioxo-2,6-diazabicyclo[5.2.0]non-1(7)-en-2-yl)ethyl]- (9CI) (CA INDEX NAME)



RN 780765-59-5 CAPLUS

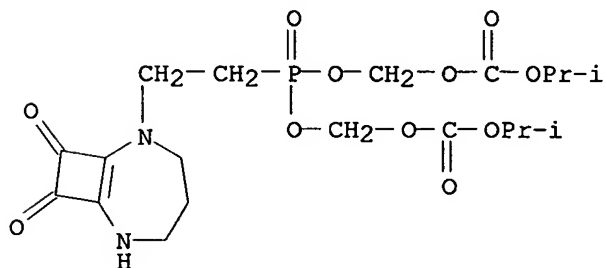
CN Phosphonic acid, [2-(8,9-dioxo-2,6-diazabicyclo[5.2.0]non-1(7)-en-2-yl)ethyl]-, bis[(benzyloxy)methyl] ester (9CI) (CA INDEX NAME)



a)

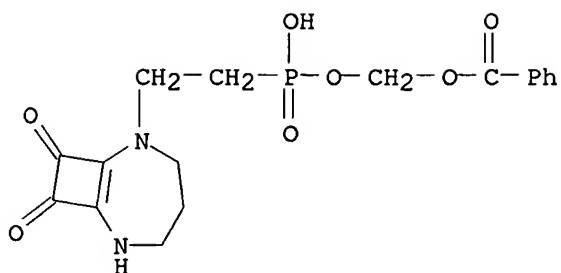
RN 780765-64-2 CAPLUS

CN 2,4,6,8-Tetraoxa-5-phosphanonanedioic acid, 5-[2-(8,9-dioxo-2,6-diazabicyclo[5.2.0]non-1(7)-en-2-yl)ethyl]-, bis(1-methylethyl) ester, 5-oxide (9CI) (CA INDEX NAME)



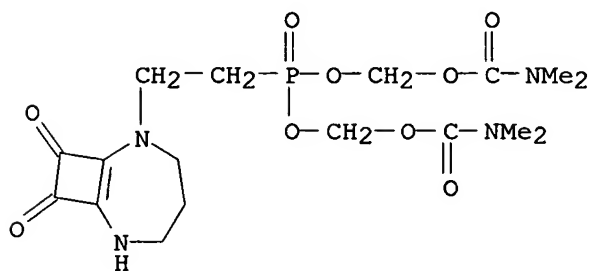
RN 780765-66-4 CAPLUS

CN Phosphonic acid, [2-(8,9-dioxo-2,6-diazabicyclo[5.2.0]non-1(7)-en-2-yl)ethyl]-, mono[(benzyloxy)methyl] ester (9CI) (CA INDEX NAME)



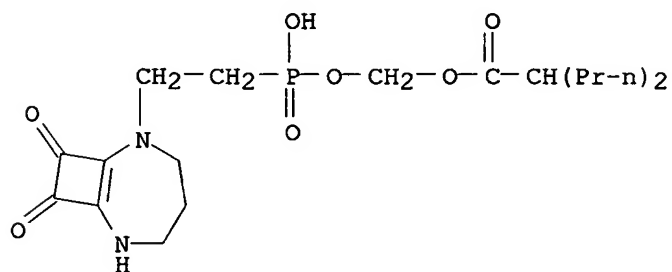
RN 780765-67-5 CAPLUS

CN Carbamic acid, dimethyl-, [[2-(8,9-dioxo-2,6-diazabicyclo[5.2.0]non-1(7)-en-2-yl)ethyl]phosphinylidene]bis(oxyethylene) ester (9CI) (CA INDEX NAME)



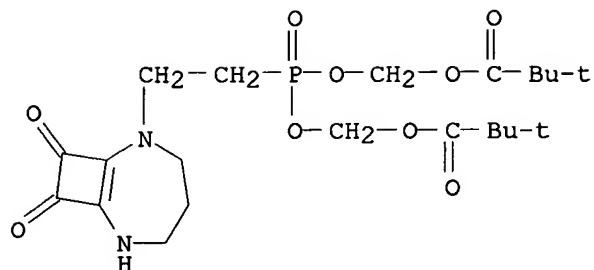
RN 782452-07-7 CAPLUS

CN Pentanoic acid, 2-propyl-, [[[2-(8,9-dioxo-2,6-diazabicyclo[5.2.0]non-1(7)-en-2-yl)ethyl]hydroxyphosphinyl]oxy]methyl ester (9CI) (CA INDEX NAME)



RN 782452-08-8 CAPLUS

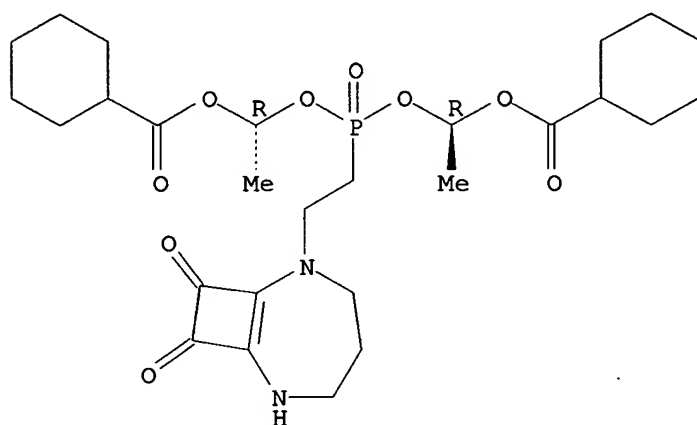
CN Propanoic acid, 2,2-dimethyl-, [[2-(8,9-dioxo-2,6-diazabicyclo[5.2.0]non-1(7)-en-2-yl)ethyl]phosphinylidene]bis(oxyethylene) ester (9CI) (CA INDEX NAME)



RN 782452-09-9 CAPLUS

CN Cyclohexanecarboxylic acid, [[2-(8,9-dioxo-2,6-diazabicyclo[5.2.0]non-1(7)-en-2-yl)ethyl]phosphinylidene]bis[oxy-(1R)-ethylidene] ester (9CI) (CA INDEX NAME)

Relative stereochemistry.

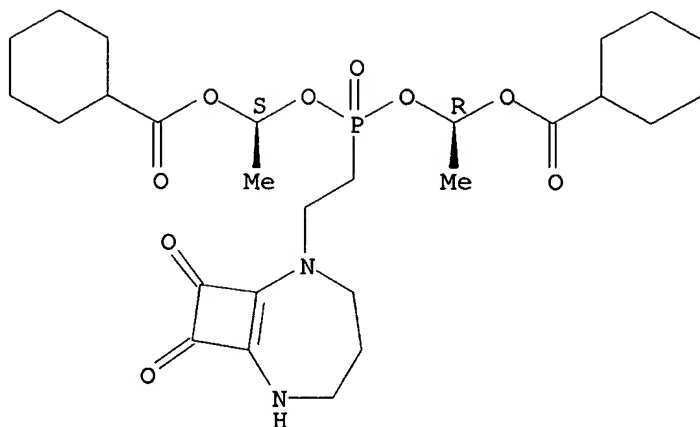


d

RN 782452-10-2 CAPLUS

CN Cyclohexanecarboxylic acid, [[2-(8,9-dioxo-2,6-diazabicyclo[5.2.0]non-1(7)-en-2-yl)ethyl]phosphinylidene]bis(oxyethylidene) ester, stereoisomer (9CI) (CA INDEX NAME)

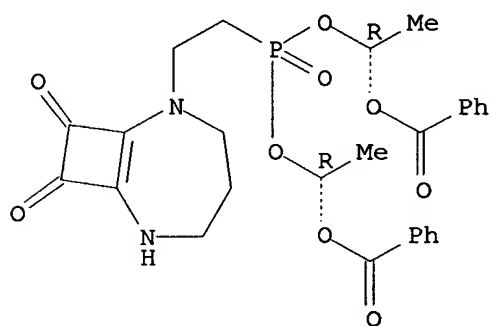
Relative stereochemistry.



RN 782452-11-3 CAPLUS

CN Phosphonic acid, [2-(8,9-dioxo-2,6-diazabicyclo[5.2.0]non-1(7)-en-2-yl)ethyl]-, bis[(1R)-1-(benzoyloxy)ethyl] ester, rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



L11 ANSWER 3 OF 17 CAPLUS COPYRIGHT 2006 ACS on STN
 ACCESSION NUMBER: 2005:371071 CAPLUS
 DOCUMENT NUMBER: 142:417206
 TITLE: Oral administration of NMDA receptor antagonists
 INVENTOR(S): Benjamin, Eric J.; Cloud, William F.; Ashraf, Muhammad; Islam, Mohammed; Brandt, Michael R.; Tremblay, Gerald F.
 PATENT ASSIGNEE(S): Wyeth, John, and Brother Ltd., USA
 SOURCE: PCT Int. Appl., 77 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 4
 PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---------------|--|----------|-----------------|----------|
| WO 2005037287 | A1 | 20050428 | WO 2004-US34113 | 20041014 |
| WO 2005037287 | C1 | 20050630 | | |
| W: | AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW | | | |
| RW: | BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | |

PRIORITY APPLN. INFO.: US 2003-511560P P 20031015
 OTHER SOURCE(S): MARPAT 142:417206

AB Solid, oral pharmaceutical dosage forms of [2-(8,9-dioxo-2,6-diazabicyclo[5.2.0]non-1(7)-en-2-yl)alkyl]phosphonic acid and its derivs. (salts) as NMDA receptor antagonists are disclosed. In addition, methods of use are disclosed for the treatment, inter alia, of cerebral vascular disorders, anxiety disorders; mood disorders; schizophrenia; schizophreniform disorder; schizoaffective disorder; cognitive impairment; chronic neurodegenerative disorders; inflammatory diseases; fibromyalgia; complications from herpes zoster; prevention of tolerance to opiate analgesia; withdrawal symptoms from addictive drugs; and pain. For example, a capsule formulation was prepared by wet granulation comprising (i) an intragranular phase containing [2-[8,9-dioxo-2,6-diazabicyclo[5.2.0]non-1(7)-en-2-yl]ethyl]phosphonic acid 100 mg, Avicel PH 101 13.91 mg, povidone 3.61 mg, and croscarmellose sodium 5.77 mg, and (ii) an extragranular phase containing Avicel PH 101 14.42 mg, croscarmellose sodium 5.77 mg, and magnesium stearate 1.44 mg.

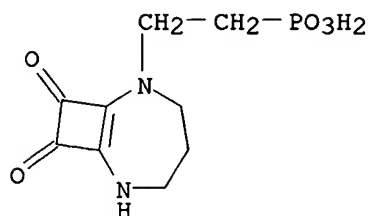
IT **144912-63-0**
 RL: PKT (Pharmacokinetics); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(preparation, bioavailability and therapeutic uses of oral compns. containing

phosphonate derivs. as NMDA antagonists)

RN 144912-63-0 CAPLUS

CN Phosphonic acid, [2-(8,9-dioxo-2,6-diazabicyclo[5.2.0]non-1(7)-en-2-yl)ethyl]- (9CI) (CA INDEX NAME)



IT 780765-59-5 780765-62-0 780765-63-1
 780765-64-2 780765-66-4 780765-67-5
 780765-68-6 782452-08-8 850148-47-9

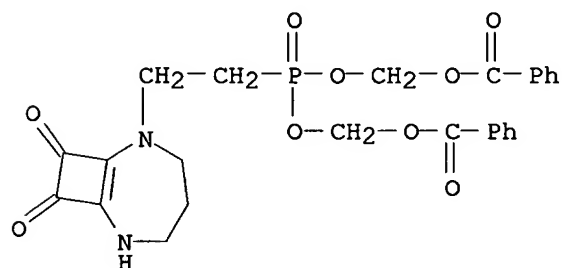
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (preparation, bioavailability and therapeutic uses of oral compns.

containing

phosphonate derivs. as NMDA antagonists)

RN 780765-59-5 CAPLUS

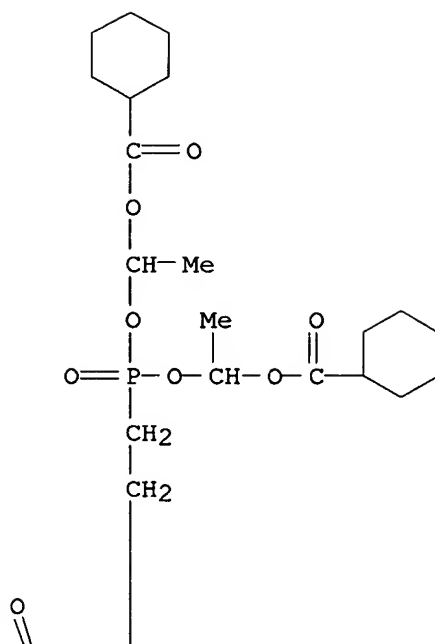
CN Phosphonic acid, [2-(8,9-dioxo-2,6-diazabicyclo[5.2.0]non-1(7)-en-2-yl)ethyl]-, bis[(benzoyloxy)methyl] ester (9CI) (CA INDEX NAME)



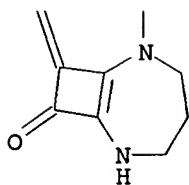
RN 780765-62-0 CAPLUS

CN Cyclohexanecarboxylic acid, [[2-(8,9-dioxo-2,6-diazabicyclo[5.2.0]non-1(7)-en-6-yl)ethyl]phosphinylidene]bis(oxyethylidene) ester (9CI) (CA INDEX NAME)

PAGE 1-A

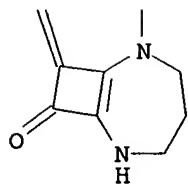
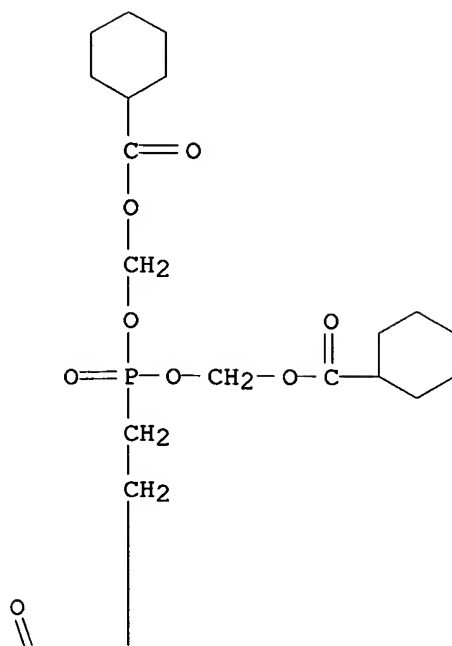


PAGE 2-A



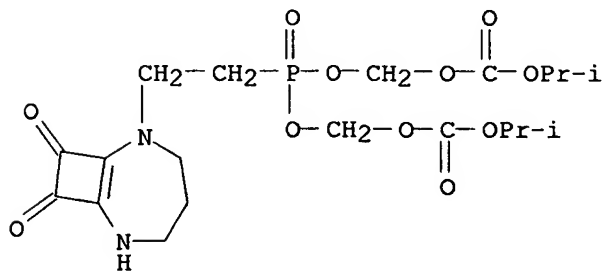
RN 780765-63-1 CAPLUS

CN Cyclohexanecarboxylic acid, [[2-(8,9-dioxo-2,6-diazabicyclo[5.2.0]non-1(7)-en-6-yl)ethyl]phosphinylidene]bis(oxyethylene) ester (9CI) (CA INDEX NAME)



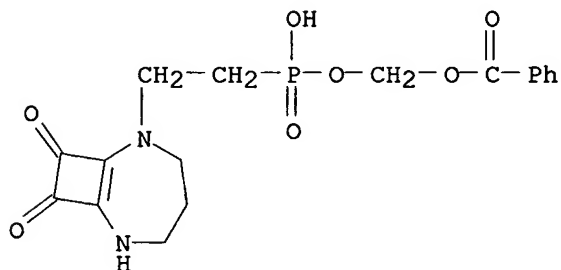
RN 780765-64-2 CAPLUS

CN 2,4,6,8-Tetraoxa-5-phosphanonanedioic acid, 5-[2-(8,9-dioxo-2,6-diazabicyclo[5.2.0]non-1(7)-en-2-yl)ethyl]-, bis(1-methylethyl) ester, 5-oxide (9CI) (CA INDEX NAME)



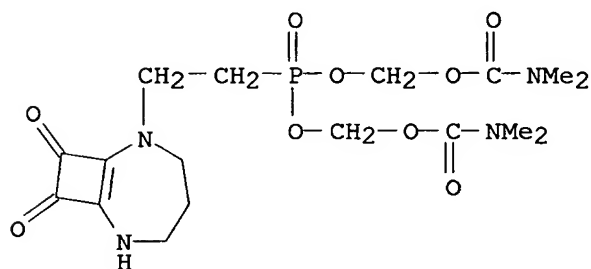
RN 780765-66-4 CAPLUS

CN Phosphonic acid, [2-(8,9-dioxo-2,6-diazabicyclo[5.2.0]non-1(7)-en-2-yl)ethyl]-, mono[(benzyloxy)methyl] ester (9CI) (CA INDEX NAME)



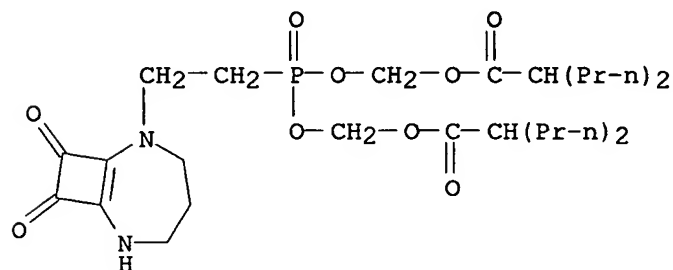
RN 780765-67-5 CAPLUS

CN Carbamic acid, dimethyl-, [[2-(8,9-dioxo-2,6-diazabicyclo[5.2.0]non-1(7)-en-2-yl)ethyl]phosphinylidene]bis(oxyethylene) ester (9CI) (CA INDEX NAME)



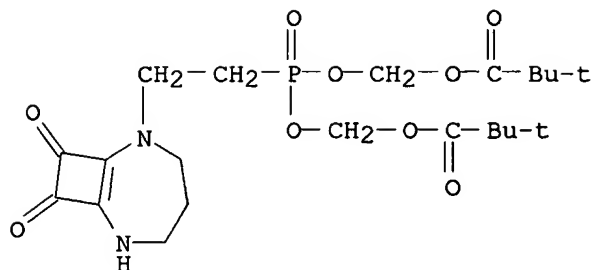
RN 780765-68-6 CAPLUS

CN Pentanoic acid, 2-propyl-, [[2-(8,9-dioxo-2,6-diazabicyclo[5.2.0]non-1(7)-en-2-yl)ethyl]phosphinylidene]bis(oxyethylene) ester (9CI) (CA INDEX NAME)



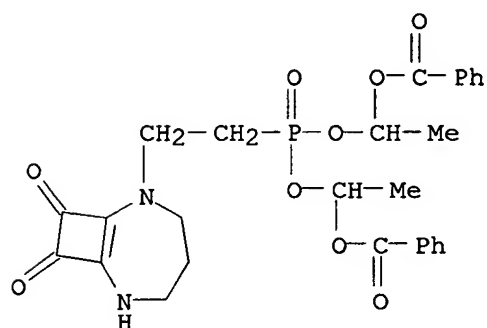
RN 782452-08-8 CAPLUS

CN Propanoic acid, 2,2-dimethyl-, [[2-(8,9-dioxo-2,6-diazabicyclo[5.2.0]non-1(7)-en-2-yl)ethyl]phosphinylidene]bis(oxyethylene) ester (9CI) (CA INDEX NAME)



RN 850148-47-9 CAPLUS

CN Phosphonic acid, [2-(8,9-dioxo-2,6-diazabicyclo[5.2.0]non-1(7)-en-2-yl)ethyl]-, bis[1-(benzoyloxy)ethyl] ester (9CI) (CA INDEX NAME)



REFERENCE COUNT:

2

THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 4 OF 17 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2005:371019 CAPLUS

DOCUMENT NUMBER: 142:411486

TITLE: Preparation of {2-[8,9-dioxo-2,6-diazabicyclo[5.2.0]non-1(7)-en-2-yl]ethyl}phosphonate esters by cyclocondensation reaction of squaric acid derivatives with (aminopropyl)aminoethanephosphonate esters and subsequent hydrolysis to free acid

INVENTOR(S): Wilk, Bogdan K.; Vid, Galina; Liu, Weiguo; Shi, Xinxu

PATENT ASSIGNEE(S): Wyeth, John, and Brother Ltd., USA

SOURCE: U.S. Pat. Appl. Publ., 10 pp.

CODEN: USXXCO

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

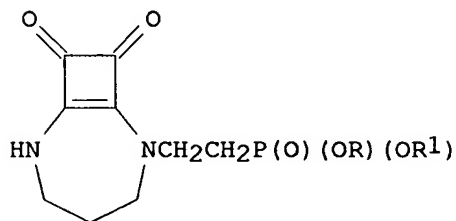
| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|------|----------|-----------------|----------|
| US 2005090470 | A1 | 20050428 | US 2004-969715 | 20041020 |
| WO 2005040176 | A2 | 20050506 | WO 2004-US34831 | 20041020 |
| WO 2005040176 | A3 | 20051201 | | |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW | | | | |
| RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |

PRIORITY APPLN. INFO.:

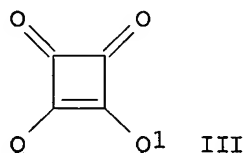
US 2003-513611P P 20031022

OTHER SOURCE(S): CASREACT 142:411486; MARPAT 142:411486

GI



I



III

AB {2-[8,9-Dioxo-2,6-diazabicyclo[5.2.0]non-1(7)-en-2-yl]ethyl}phosphonic acid (I; R = R₁ = H), useful as an NMDA antagonist appropriate for treatment of stroke, epilepsy, Alzheimer's and Parkinson's diseases and pain (no data), is prepared by hydrolysis of its esters I (R, R₁ = C₁-6 alkyl, C₁-6 haloalkyl; preferably R = R₁ = Et), which in turn are prepared by reaction of a 1,3-diaminopropane derivative H₂N(CH₂)₃NHCH₂CH₂P(O)(OR)(OR₁) (II; same R, R₁) with a cyclobutenedione (III; Q, Q₁ = OH, halo, OX₁;

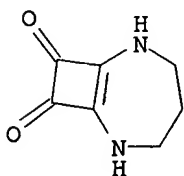
preferably Q, Q1 = OEt or OH; X1 = C1-6 alkyl, C1-6 haloalkyl, aryl) in a solvent HOX1 (same X1; preferably HOX1 = MeOH or EtOH); compds. II are prepared by reaction of 1,3-diaminopropane with XCH₂CH₂P(O)(OR)(OR1) or CH₂:CHP(O)(OR)(OR1) (same R, R1; X = leaving group, preferably halo) at a ratio of $\geq 2:1$. In an example, treating 1.04 g di-Et squarate III (Q = Q1 = OEt) in 250 mL MeOH with 1.46 g II (R = R1 = Et; preparation given.) in 50 mL MeOH at 60° for 6 h and subsequent stirring overnight at room temperature gave 54% title ester I (R = R1 = Et).

IT **66086-41-7P**

RL: BYP (Byproduct); SPN (Synthetic preparation); PREP (Preparation)
(preparation of [[dioxodiazabicyclo[5.2.0]nonenyl]ethyl]phosphonates by cyclocondensation reaction of squaric acid derivs. with diaminopropane phosphonate derivs. and hydrolysis to give free acid)

RN 66086-41-7 CAPLUS

CN 2,6-Diazabicyclo[5.2.0]non-1(7)-ene-8,9-dione (9CI) (CA INDEX NAME)

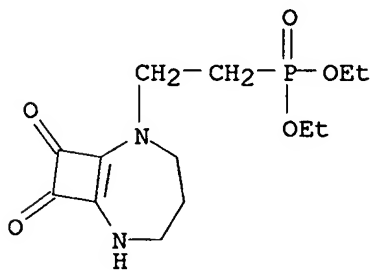


IT **144912-83-4P**

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of [[dioxodiazabicyclo[5.2.0]nonenyl]ethyl]phosphonates by cyclocondensation reaction of squaric acid derivs. with diaminopropane phosphonate derivs. and hydrolysis to give free acid)

RN 144912-83-4 CAPLUS

CN Phosphonic acid, [2-(8,9-dioxo-2,6-diazabicyclo[5.2.0]non-1(7)-en-2-yl)ethyl]-, diethyl ester (9CI) (CA INDEX NAME)



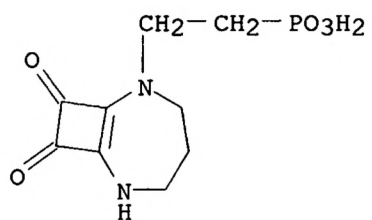
IT **144912-63-0P**

RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of [[dioxodiazabicyclo[5.2.0]nonenyl]ethyl]phosphonates by cyclocondensation reaction of squaric acid derivs. with diaminopropane phosphonate derivs. and hydrolysis to give free acid)

RN 144912-63-0 CAPLUS

CN Phosphonic acid, [2-(8,9-dioxo-2,6-diazabicyclo[5.2.0]non-1(7)-en-2-yl)ethyl]- (9CI) (CA INDEX NAME)

10/820,215



L11 ANSWER 5 OF 17 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2004:902398 CAPLUS

DOCUMENT NUMBER: 141:380023

TITLE: Preparation of derivatives of 2-(8,9-dioxo-2,6-diazabicyclo(5.2.0)non-1(7)-en-2-yl)alkylphosphonic acid and their use as n-methyl-d-aspartate (nmda) receptor antagonists

INVENTOR(S): Baudy, Reinhardt Bernhard; Butera, John Anthony

PATENT ASSIGNEE(S): Wyeth, John, and Brother Ltd., USA

SOURCE: PCT Int. Appl., 52 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

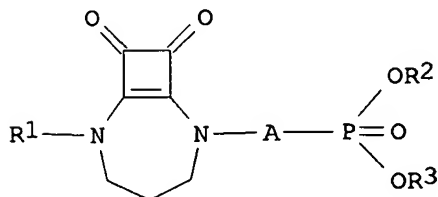
LANGUAGE: English

FAMILY ACC. NUM. COUNT: 4

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------------------------|--|--|-----------------|------------|
| WO 2004092189 | A1 | 20041028 | WO 2004-US10596 | 20040407 |
| W: | AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW | | | |
| RW: | BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | |
| CA 2521313 | AA | 20041028 | CA 2004-2521313 | 20040407 |
| EP 1611144 | A1 | 20060104 | EP 2004-759168 | 20040407 |
| R: | AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK, HR | | | |
| PRIORITY APPLN. INFO.: | | | US 2003-461490P | P 20030409 |
| | | | WO 2004-US10596 | W 20040407 |
| OTHER SOURCE(S): | | CASREACT 141:380023; MARPAT 141:380023 | | |

GI



I

AB Preparation of title compds. I (at least one R2 or R3 is not hydrogen; R1 = H, C1-6 alkyl, C2-7 acyl, C1-6 alkanesulfonyl, C6-14 aroyl; R2, R3 = H, (un)substituted alkylcarboxyalkyl, alkoxycarboxyalkyl, aminocarboxyalkyl; A = C1-4 alkylene, C2-4 alkenylene) or pharmaceutically acceptable salts

thereof are provided. The compds. of the present invention are N-methyl-D-aspartate (NMDA) receptor antagonists and are useful in treating a variety of conditions present in a mammal that benefit from inhibiting the NMDA receptor. Thus, reaction of [2-(8,9-dioxo-2,6-diazabicyclo[5.2.0]non-1(7)-en-2-yl)ethyl]phosphonic acid with benzoic acid chloromethyl ester in DMF in the presence of N,N-diisopropylethylamine gave 99% title compound, 3-{2-[8,9-dioxo-2,6-diazabicyclo[5.2.0]non-1(7)-en-2-yl]ethyl}-3-oxido-7-oxo-7-phenyl-2,4,6-trioxa-3-phosphahept-1-yl benzoate.

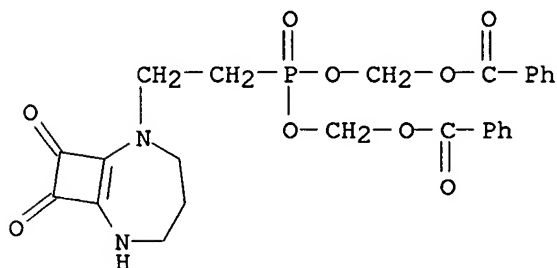
IT **780765-59-5P**

RL: BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)

(preparation of derivs. of dioxodiazabicyclononenalkylphosphonic acid and their use as Me aspartate NMDA receptor antagonists)

RN 780765-59-5 CAPLUS

CN Phosphonic acid, [2-(8,9-dioxo-2,6-diazabicyclo[5.2.0]non-1(7)-en-2-yl)ethyl]-, bis[(benzoyloxy)methyl] ester (9CI) (CA INDEX NAME)



IT **780765-63-1P 780765-64-2P 780765-66-4P**

780765-67-5P 782452-07-7P 782452-08-8P

782452-09-9P 782452-10-2P 782452-11-3P

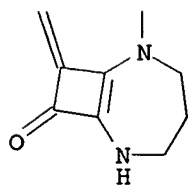
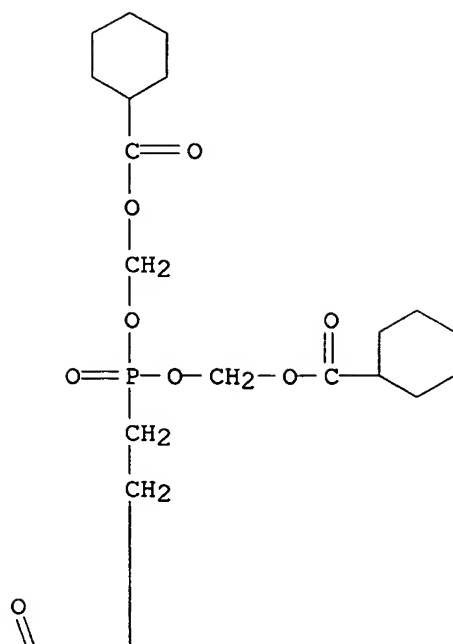
782452-12-4P

RL: BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of derivs. of dioxodiazabicyclononenalkylphosphonic acid and their use as Me aspartate NMDA receptor antagonists)

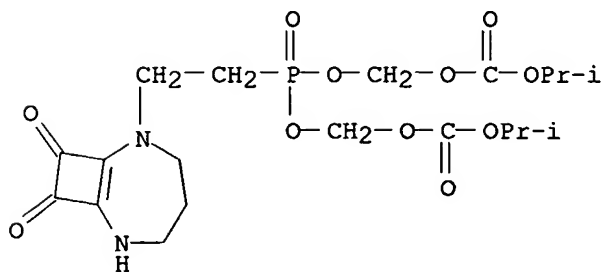
RN 780765-63-1 CAPLUS

CN Cyclohexanecarboxylic acid, [[2-(8,9-dioxo-2,6-diazabicyclo[5.2.0]non-1(7)-en-6-yl)ethyl]phosphinylidene]bis(oxymethylene) ester (9CI) (CA INDEX NAME)



RN 780765-64-2 CAPLUS

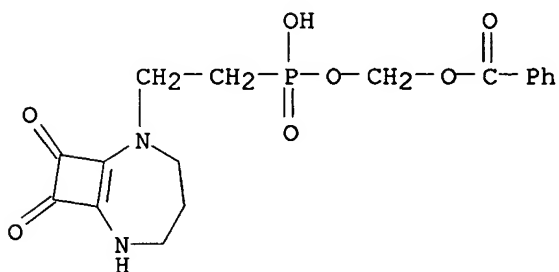
CN 2,4,6,8-Tetraoxa-5-phosphanonanedioic acid, 5-[2-(8,9-dioxo-2,6-diazabicyclo[5.2.0]non-1(7)-en-2-yl)ethyl]-, bis(1-methylethyl) ester, 5-oxide (9CI) (CA INDEX NAME)



10/820,215

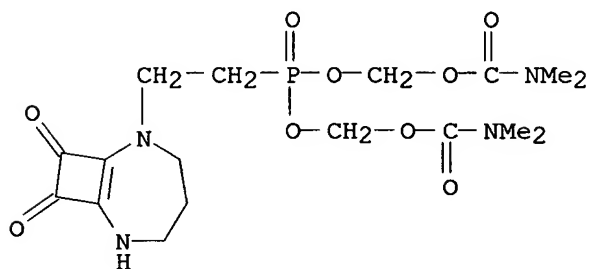
RN 780765-66-4 CAPLUS

CN Phosphonic acid, [2-(8,9-dioxo-2,6-diazabicyclo[5.2.0]non-1(7)-en-2-yl)ethyl]-, mono[(benzoyloxy)methyl] ester (9CI) (CA INDEX NAME)



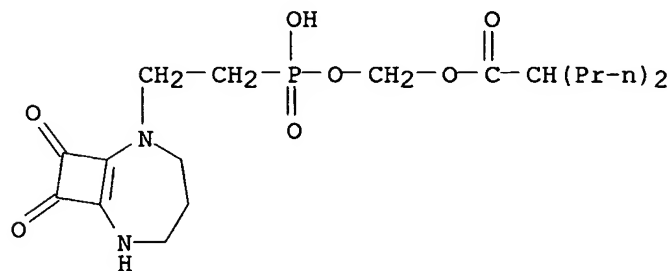
RN 780765-67-5 CAPLUS

CN Carbamic acid, dimethyl-, [[2-(8,9-dioxo-2,6-diazabicyclo[5.2.0]non-1(7)-en-2-yl)ethyl]phosphinylidene]bis(oxymethylene) ester (9CI) (CA INDEX NAME)



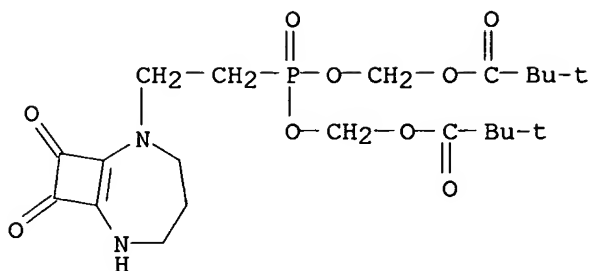
RN 782452-07-7 CAPLUS

CN Pentanoic acid, 2-propyl-, [[[2-(8,9-dioxo-2,6-diazabicyclo[5.2.0]non-1(7)-en-2-yl)ethyl]hydroxyphosphinyl]oxy]methyl ester (9CI) (CA INDEX NAME)



RN 782452-08-8 CAPLUS

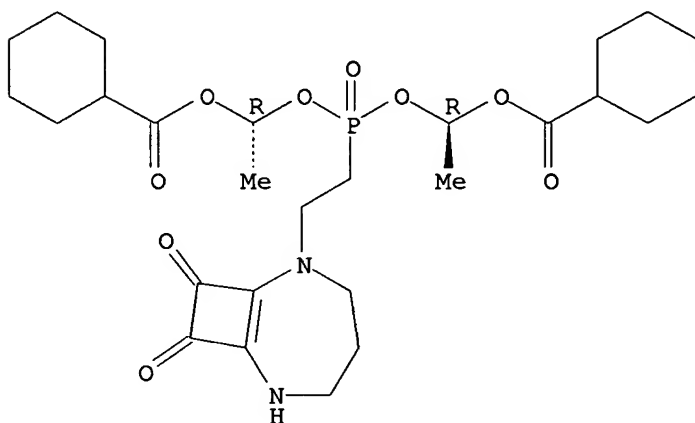
CN Propanoic acid, 2,2-dimethyl-, [[2-(8,9-dioxo-2,6-diazabicyclo[5.2.0]non-1(7)-en-2-yl)ethyl]phosphinylidene]bis(oxymethylene) ester (9CI) (CA INDEX NAME)



RN 782452-09-9 CAPLUS

CN Cyclohexanecarboxylic acid, [[2-(8,9-dioxo-2,6-diazabicyclo[5.2.0]non-1(7)-en-2-yl)ethyl]phosphinyldene]bis[oxy-(1R)-ethylidene] ester (9CI) (CA INDEX NAME)

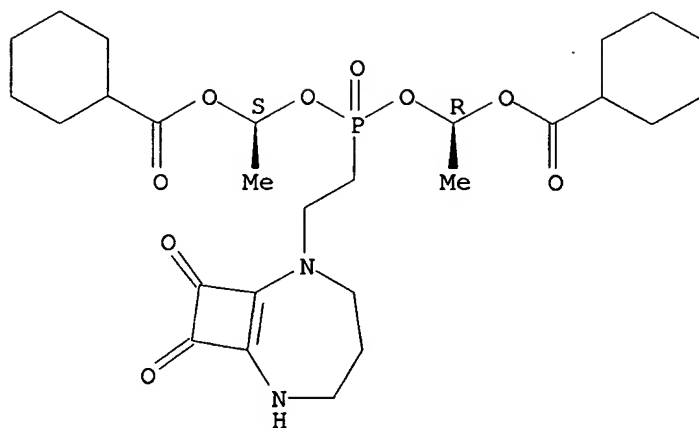
Relative stereochemistry.



RN 782452-10-2 CAPLUS

CN Cyclohexanecarboxylic acid, [[2-(8,9-dioxo-2,6-diazabicyclo[5.2.0]non-1(7)-en-2-yl)ethyl]phosphinyldene]bis(oxyethylidene) ester, stereoisomer (9CI) (CA INDEX NAME)

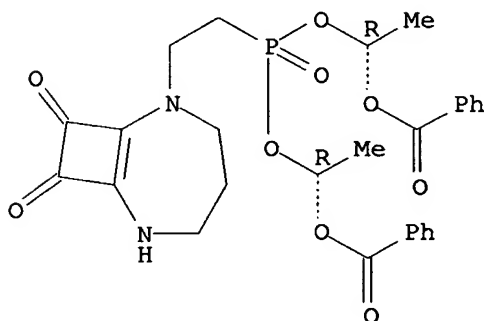
Relative stereochemistry.



RN 782452-11-3 CAPLUS

CN Phosphonic acid, [2-(8,9-dioxo-2,6-diazabicyclo[5.2.0]non-1(7)-en-2-yl)ethyl]-, bis[(1R)-1-(benzoyloxy)ethyl] ester, rel- (9CI) (CA INDEX NAME)

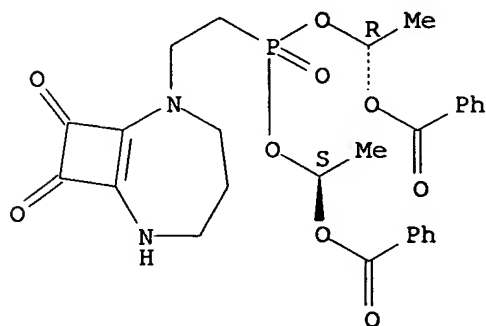
Relative stereochemistry.



RN 782452-12-4 CAPLUS

CN Phosphonic acid, [2-(8,9-dioxo-2,6-diazabicyclo[5.2.0]non-1(7)-en-2-yl)ethyl]-, (1R)-1-(benzoyloxy)ethyl (1S)-1-(benzoyloxy)ethyl ester, rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



10/820,215

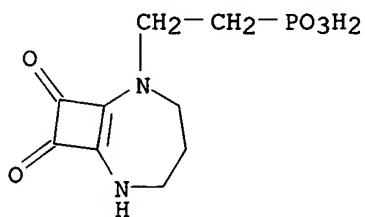
IT **144912-63-0**

RL: RCT (Reactant); RACT (Reactant or reagent)

(preparation of derivs. of dioxodiazabicyclononenalkylphosphonic acid and their use as Me aspartate NMDA receptor antagonists)

RN 144912-63-0 CAPLUS

CN Phosphonic acid, [2-(8,9-dioxo-2,6-diazabicyclo[5.2.0]non-1(7)-en-2-yl)ethyl]- (9CI) (CA INDEX NAME)



REFERENCE COUNT:

22

THERE ARE 22 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 6 OF 17 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2004:902198 CAPLUS

DOCUMENT NUMBER: 141:370576

TITLE: Intranasal pharmaceutical compositions containing [2-(8,9-dioxo-2,6-diazabicyclo[5.2.0]non-1(7)-en-2-yl)alkyl]phosphonic acid and its derivatives

INVENTOR(S): Benjamin, Eric Joel; Baudy, Reinhardt Bernhard; Brandt, Michael Richard

PATENT ASSIGNEE(S): Wyeth, John, and Brother Ltd., USA

SOURCE: PCT Int. Appl., 46 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 4

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------------------------|--|----------|-----------------|------------|
| WO 2004091633 | A1 | 20041028 | WO 2004-US11668 | 20040407 |
| WO 2004091633 | C1 | 20050113 | | |
| W: | AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW | | | |
| RW: | BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | |
| CA 2521394 | AA | 20041028 | CA 2004-2521394 | 20040407 |
| EP 1622625 | A1 | 20060208 | EP 2004-759562 | 20040407 |
| R: | AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK, HR | | | |
| PRIORITY APPLN. INFO.: | | | US 2003-461571P | P 20030409 |
| | | | WO 2004-US11668 | W 20040407 |

OTHER SOURCE(S): MARPAT 141:370576

AB Pharmaceutical compns. for intranasal administration contain the title compound or a salt thereof, and 1 or more additives for forming a composition for

intranasal administration. Also provided are methods of treating conditions in a mammal associated with a glutamate abnormality that includes administering intranasally to a mammal a therapeutically effective amount of the above compds. Thus, a nasal solution contained [2-(8,9-dioxo-2,6-diazabicyclo[5.2.0]non-1(7)-en-2-yl)ethyl]phosphonic acid 30.0 and EDTA 0.10 g, 5N NaOH solution 37 and water 50 mL.

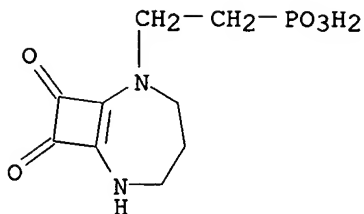
IT 144912-63-0

RL: PKT (Pharmacokinetics); RCT (Reactant); THU (Therapeutic use); BIOL (Biological study); RACT (Reactant or reagent); USES (Uses)

(intranasal pharmaceutical compns. containing dioxo(diazabicyclononyl)alkylphosphonic acid and its derivs.)

RN 144912-63-0 CAPLUS

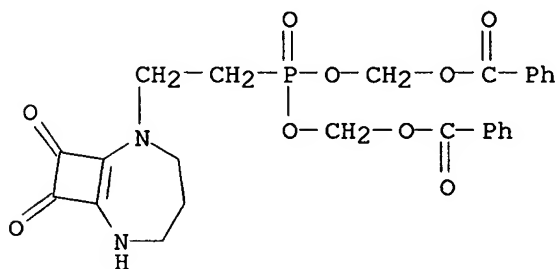
CN Phosphonic acid, [2-(8,9-dioxo-2,6-diazabicyclo[5.2.0]non-1(7)-en-2-yl)ethyl]- (9CI) (CA INDEX NAME)

IT **780765-59-5P**

RL: PKT (Pharmacokinetics); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(intranasal pharmaceutical compns. containing dioxo(diazabicyclononyl)alkylphosphonic acid and its derivs.)

RN 780765-59-5 CAPLUS

CN Phosphonic acid, [2-(8,9-dioxo-2,6-diazabicyclo[5.2.0]non-1(7)-en-2-yl)ethyl]-, bis[(benzoyloxy)methyl] ester (9CI) (CA INDEX NAME)



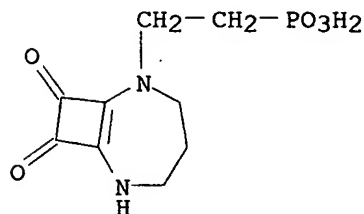
a)

IT **780765-60-8 780765-61-9 780765-62-0****780765-63-1 780765-64-2 780765-65-3****780765-66-4 780765-67-5 780765-68-6**

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(intranasal pharmaceutical compns. containing dioxo(diazabicyclononyl)alkylphosphonic acid and its derivs.)

RN 780765-60-8 CAPLUS

CN Phosphonic acid, [2-(8,9-dioxo-2,6-diazabicyclo[5.2.0]non-1(7)-en-2-yl)ethyl]-, sodium salt (9CI) (CA INDEX NAME)

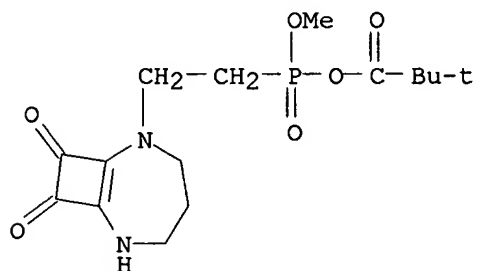


●x Na

10/820,215

RN 780765-61-9 CAPLUS

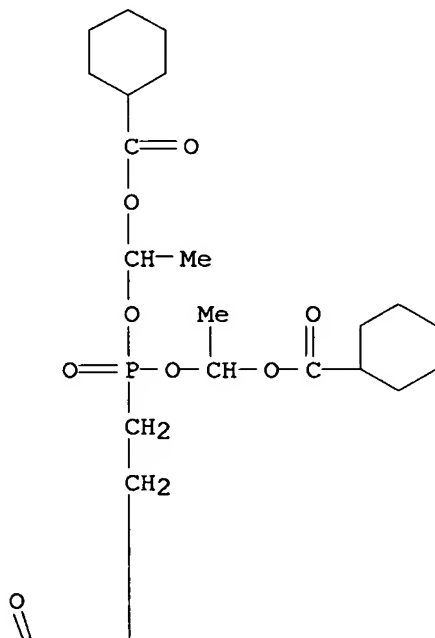
CN Propanoic acid, 2,2-dimethyl-, anhydride with methyl hydrogen
[2-(8,9-dioxo-2,6-diazabicyclo[5.2.0]non-1(7)-en-2-yl)ethyl]phosphonate
(9CI) (CA INDEX NAME)



c)

RN 780765-62-0 CAPLUS

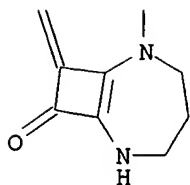
CN Cyclohexanecarboxylic acid, [[2-(8,9-dioxo-2,6-diazabicyclo[5.2.0]non-1(7)-
en-6-yl)ethyl]phosphinylidene]bis(oxyethylidene) ester (9CI) (CA INDEX
NAME)



d)

PAGE 1-A

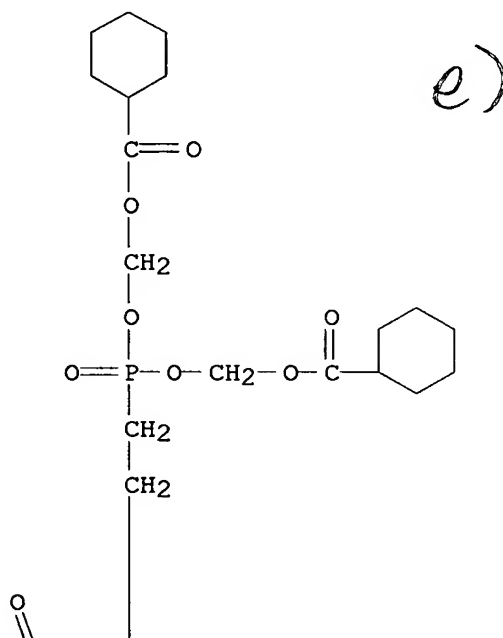
PAGE 2-A



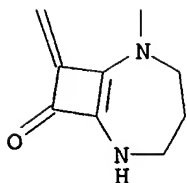
RN 780765-63-1 CAPLUS

CN Cyclohexanecarboxylic acid, [[2-(8,9-dioxo-2,6-diazabicyclo[5.2.0]non-1(7)-en-6-yl)ethyl]phosphinyldene]bis(oxyethylene) ester (9CI) (CA INDEX NAME)

PAGE 1-A



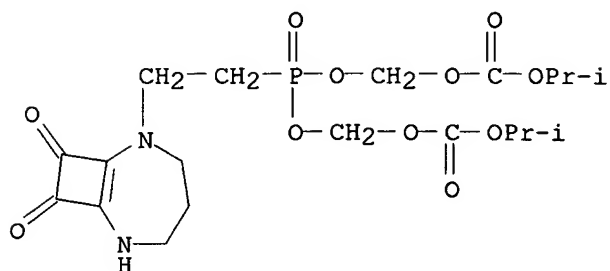
PAGE 2-A



RN 780765-64-2 CAPLUS

CN 2,4,6,8-Tetraoxa-5-phosphanonanedioic acid, 5-[2-(8,9-dioxo-2,6-

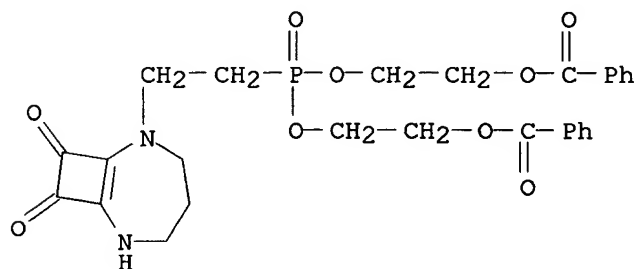
diazabicyclo[5.2.0]non-1(7)-en-2-yl)ethyl]-, bis(1-methylethyl) ester, 5-oxide (9CI) (CA INDEX NAME)



f)

RN 780765-65-3 CAPLUS

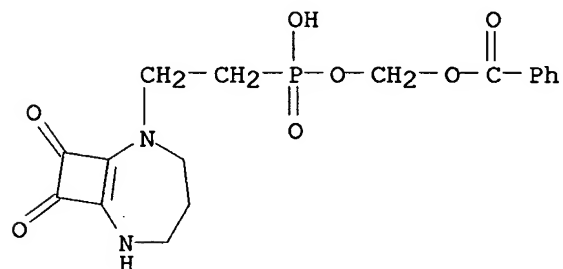
CN Phosphonic acid, [2-(8,9-dioxo-2,6-diazabicyclo[5.2.0]non-1(7)-en-2-yl)ethyl]-, bis[2-(benzoyloxy)ethyl] ester (9CI) (CA INDEX NAME)



g)

RN 780765-66-4 CAPLUS

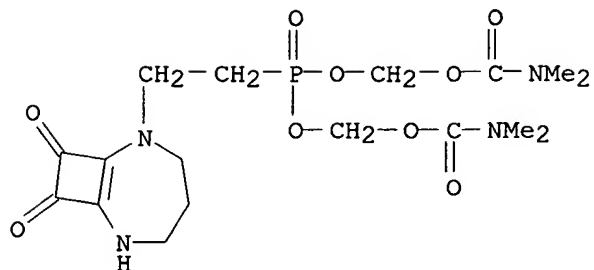
CN Phosphonic acid, [2-(8,9-dioxo-2,6-diazabicyclo[5.2.0]non-1(7)-en-2-yl)ethyl]-, mono[(benzoyloxy)methyl] ester (9CI) (CA INDEX NAME)



h)

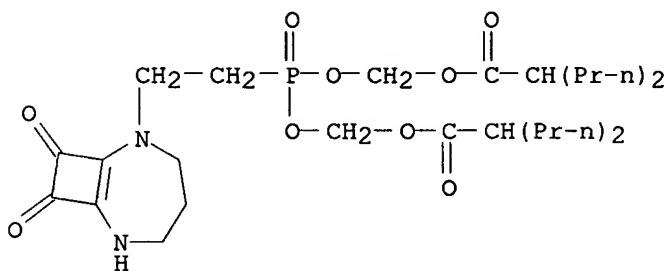
RN 780765-67-5 CAPLUS

CN Carbamic acid, dimethyl-, [[2-(8,9-dioxo-2,6-diazabicyclo[5.2.0]non-1(7)-en-2-yl)ethyl]phosphinylidene]bis(oxyethylene) ester (9CI) (CA INDEX NAME)



RN 780765-68-6 CAPLUS

CN Pentanoic acid, 2-propyl-, [[2-(8,9-dioxo-2,6-diazabicyclo[5.2.0]non-1(7)-en-2-yl)ethyl]phosphinyldiene]bis(oxyethylene) ester (9CI) (CA INDEX NAME)



REFERENCE COUNT:

4

THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 7 OF 17 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2003:301059 CAPLUS

DOCUMENT NUMBER: 138:314606

TITLE: [[2-(amino-3,4-dioxo-1-cyclobuten-1-yl)amino]alkyl]-
acid derivatives for the treatment of painINVENTOR(S): Brandt, Michael Richard; Zaleska, Margaret Maria;
Moyer, John Allen

PATENT ASSIGNEE(S): Wyeth, John, and Brother Ltd., USA

SOURCE: PCT Int. Appl., 40 pp.

CODEN: PIXXD2

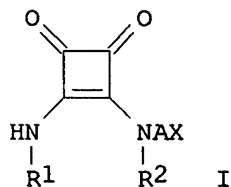
DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|------|-------------------|-----------------|------------|
| WO 2003031416 | A2 | 20030417 | WO 2002-US32252 | 20021009 |
| WO 2003031416 | A3 | 20030814 | | |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW | | | | |
| RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |
| CA 2461348 | AA | 20030417 | CA 2002-2461348 | 20021009 |
| US 2003114444 | A1 | 20030619 | US 2002-267159 | 20021009 |
| EP 1434588 | A2 | 20040707 | EP 2002-789180 | 20021009 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK | | | | |
| BR 2002013237 | A | 20040928 | BR 2002-13237 | 20021009 |
| JP 2005508950 | T2 | 20050407 | JP 2003-534400 | 20021009 |
| NO 2004001378 | A | 20040528 | NO 2004-1378 | 20040402 |
| PRIORITY APPLN. INFO.: | | | US 2001-328245P | P 20011010 |
| | | | WO 2002-US32252 | W 20021009 |
| OTHER SOURCE(S): | | MARPAT 138:314606 | | |
| GI | | | | |



AB The invention provides a method for treating pain in a mammal that includes administering I [R1 = H, C1-6 alkyl, C7-12 phenylalkyl; R2 = H, C1-6 alkyl, C2-6 alkenyl, C7-12 phenylalkyl; or R1 and R2 taken together

as Z are CH₂CH₂, CH₂C(R₆)(R₇)CH₂, CH₂C(R₈)(R₉)C(R₁₀)(R₁₁)CH₂; R₆, R₈, R₁₀ = H, C1-6 alkyl, OH; R₇, R₉, R₁₁ = H, C1-6 alkyl; A = C1-6 alkylene, C2-6 alkenylene; X = CO₂R₃, P(O)(OR₄)(OR₅), 3,5-dioxo-1,2,4-oxadiazolidin-2-yl, 5-tetrazolyl; R₃, R₄, R₅ = H, C1-6 alkyl], or a pharmaceutically acceptable salt thereof. Also provided are compns. for treating pain containing I.

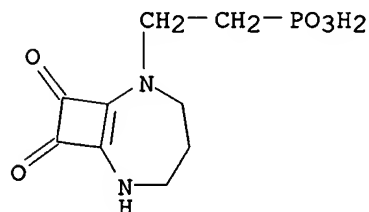
IT 144912-63-0 144912-64-1 144912-67-4

144912-69-6

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(aminodioxocyclobutenyl derivs. for treatment of pain)

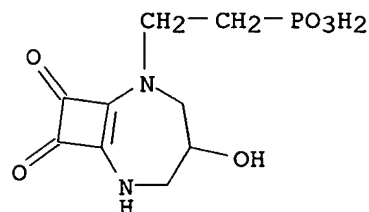
RN 144912-63-0 CAPLUS

CN Phosphonic acid, [2-(8,9-dioxo-2,6-diazabicyclo[5.2.0]non-1(7)-en-2-yl)ethyl]- (9CI) (CA INDEX NAME)



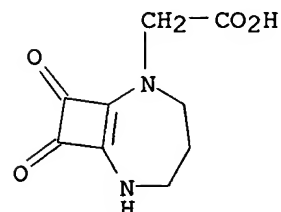
RN 144912-64-1 CAPLUS

CN Phosphonic acid, [2-(4-hydroxy-8,9-dioxo-2,6-diazabicyclo[5.2.0]non-1(7)-en-2-yl)ethyl]- (9CI) (CA INDEX NAME)



RN 144912-67-4 CAPLUS

CN 2,6-Diazabicyclo[5.2.0]non-1(7)-ene-2-acetic acid, 8,9-dioxo- (9CI) (CA INDEX NAME)

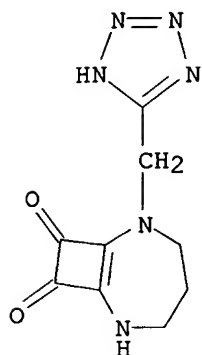


RN 144912-69-6 CAPLUS

CN 2,6-Diazabicyclo[5.2.0]non-1(7)-ene-8,9-dione, 2-(1H-tetrazol-5-ylmethyl)-

10/820,215

(9CI) (CA INDEX NAME)



111 ANSWER 8 OF 17 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1999:748347 CAPLUS

DOCUMENT NUMBER: 131:337040

TITLE: Preparation of [2-(8,9-dioxo-2,6-diazabicyclo[5.2.0]non-1(7)-en-2-yl)ethyl]phosphonic acid

INVENTOR(S): Asselin, Andre A.; Kinney, William A.; Schmid, Jean

PATENT ASSIGNEE(S): American Home Products Corporation, USA

SOURCE: U.S., 6 pp.

CODEN: USXXAM

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------------------------|------|----------|-----------------|-------------|
| US 5990307 | A | 19991123 | US 1998-127202 | 19980731 |
| US 6011168 | A | 20000104 | US 1999-375345 | 19990816 |
| PRIORITY APPLN. INFO.: | | | US 1997-54553P | P 19970801 |
| | | | US 1998-127202 | A3 19980731 |

OTHER SOURCE(S): CASREACT 131:337040

AB [2-(8,9-Dioxo-2,6-diazabicyclo[5.2.0]non-1(7)-en-2-yl)ethyl]phosphonic acid (I) was prepared by reaction of Me₃CO₂CNH(CH₂)₃NH₂ with a dialkyl vinylphosphonate to obtain N-[3-(t-butyloxycarbonylamino)propyl]-2-aminoethylphosphonic acid dialkyl ester in 80% yield. Reaction of the latter with a 3,4-dialkoxycyclobut-3-en-1,2-dione gave [3-[[2-(dialkoxyphosphoryl)ethyl]-(2-alkoxy-3,4-dioxo-1,2-cyclobuten-1-yl)amino]propyl]carbamic acid 1,1-dimethylethyl ester in 96% yield. Deprotection and cyclization of this in CF₃CO₂H gave [2-((8,9)-dioxo-2,6-diazabicyclo[5.2.0]-non-1(7)-en-2-yl)ethyl]phosphonic acid dialkyl ester in 58% yield; treatment with BrSiMe₃ gave I in 38.8% overall yield.

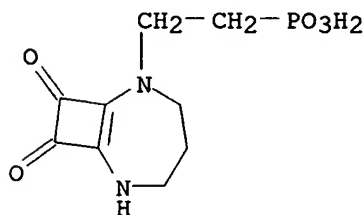
IT **144912-63-0P**

RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)

(preparation of [2-(8,9-dioxo-2,6-diazabicyclo[5.2.0]non-1(7)-en-2-yl)ethyl]phosphonic acid)

RN 144912-63-0 CAPLUS

CN Phosphonic acid, [2-(8,9-dioxo-2,6-diazabicyclo[5.2.0]non-1(7)-en-2-yl)ethyl]- (9CI) (CA INDEX NAME)



IT **144912-83-4P**

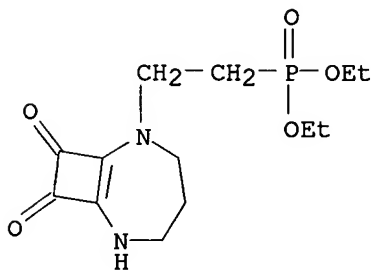
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation of [2-(8,9-dioxo-2,6-diazabicyclo[5.2.0]non-1(7)-en-2-yl)ethyl]phosphonic acid)

RN 144912-83-4 CAPLUS

10/820,215

CN Phosphonic acid, [2-(8,9-dioxo-2,6-diazabicyclo[5.2.0]non-1(7)-en-2-yl)ethyl]-, diethyl ester (9CI) (CA INDEX NAME)



REFERENCE COUNT:

3

THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

10/820,215

111 ANSWER 9 OF 17 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1999:113692 CAPLUS

DOCUMENT NUMBER: 130:153793

TITLE: Preparation of [2-(8,9-dioxo-2,6-diazabicyclo[5.2.0]non-1(7)-en-2-yl)ethyl]phosphonic acid

INVENTOR(S): Asselin, Andre Alfred; Kinney, William Alvin; Schmid, Jean

PATENT ASSIGNEE(S): American Home Products Corporation, USA

SOURCE: PCT Int. Appl., 17 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------------------------|--|----------|------------------|------------|
| WO 9906417 | A1 | 19990211 | WO 1998-US15841 | 19980731 |
| W: | AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | |
| RW: | GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG | | | |
| CA 2297411 | AA | 19990211 | CA 1998-2297411 | 19980731 |
| AU 9886037 | A1 | 19990222 | AU 1998-86037 | 19980731 |
| AU 746119 | B2 | 20020418 | | |
| EP 1000072 | A1 | 20000517 | EP 1998-937292 | 19980731 |
| EP 1000072 | B1 | 20030219 | | |
| R: | AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, SI, LT, LV, FI, RO | | | |
| BR 9811807 | A | 20000815 | BR 1998-11807 | 19980731 |
| JP 2001512129 | T2 | 20010821 | JP 2000-505174 | 19980731 |
| NZ 502509 | A | 20020828 | NZ 1998-502509 | 19980731 |
| AT 232875 | E | 20030315 | AT 1998-937292 | 19980731 |
| RU 2205834 | C2 | 20030610 | RU 2000-105273 | 19980731 |
| ES 2190091 | T3 | 20030716 | ES 1998-937292 | 19980731 |
| CN 1526714 | A | 20040908 | CN 2003-10120120 | 19980731 |
| NO 2000000488 | A | 20000131 | NO 2000-488 | 20000131 |
| HK 1027814 | A1 | 20030516 | HK 2000-107097 | 20001108 |
| PRIORITY APPLN. INFO.: | | | US 1997-905091 | A 19970801 |
| | | | WO 1998-US15841 | W 19980731 |

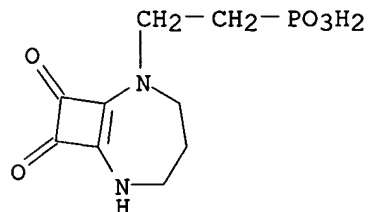
AB The title compound (I), an NMDA antagonist, was useful as an anticonvulsant and neuroprotectant in situations involving excess release of excitatory amino acids. 3-Aminopropylcarbamate acid 1,1-dimethyl-Et ester was treated with a dialkyl vinylphosphonate (alkyl = Me, Et) to obtain N-[3-(tert-butyloxycarbonylamino)propyl]-2-aminoethylphosphonic acid dialkyl ester (II) in 80% yield. Reaction of II with 3,4-diethoxycyclobut-3-ene-1,2-dione gave [3-[[2-(dialkoxyphosphoryl)ethyl]-(2-alkoxy-3,4-dioxo-1,2-cyclobuten-1-yl)amino]propyl]carbamate acid 1,1-dimethylethyl ester (III) in 96% yield. Deprotection and cyclization of III in HO₂CCF₃ gives [2-(8,9-dioxo-2,6-diazabicyclo[5.2.0]non-1(7)-en-2-yl)ethyl]phosphonic acid dialkyl ester (IV) in 58% yield. Compound IV was treated with bromotrimethylsilane to give I.

IT 144912-63-0P

RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)

RN 144912-63-0 CAPLUS

CN Phosphonic acid, [2-(8,9-dioxo-2,6-diazabicyclo[5.2.0]non-1(7)-en-2-yl)ethyl]- (9CI) (CA INDEX NAME)

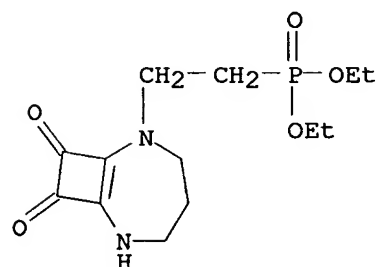


IT 144912-83-4P 220288-14-2P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
(Reactant or reagent)
(preparation of [(dioxodiazabicyclo[5.2.0]nonenyl)ethyl]phosphonic acid
esters)

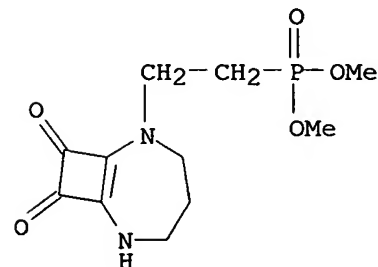
RN 144912-83-4 CAPLUS

CN Phosphonic acid, [2-(8,9-dioxo-2,6-diazabicyclo[5.2.0]non-1(7)-en-2-yl)ethyl]-, diethyl ester (9CI) (CA INDEX NAME)



RN 220288-14-2 CAPLUS

CN Phosphonic acid, [2-(8,9-dioxo-2,6-diazabicyclo[5.2.0]non-1(7)-en-2-yl)ethyl]-, dimethyl ester (9CI) (CA INDEX NAME)



REFERENCE COUNT:

1

THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 10 OF 17 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1998:9157 CAPLUS

DOCUMENT NUMBER: 128:75452

TITLE: Design and Synthesis of [2-(8,9-Dioxo-2,6-diazabicyclo[5.2.0]non-1(7)-en-2-yl)ethyl]phosphonic Acid (EAA-090), a Potent N-Methyl-D-aspartate Antagonist, via the Use of 3-Cyclobutene-1,2-dione as an Achiral α -Amino Acid Bioisostere

AUTHOR(S): Kinney, William A.; Abou-Gharbia, Magid; Garrison, Deanna T.; Schmid, Jean; Kowal, Dianne M.; Bramlett, Donna R.; Miller, Tracy L.; Tasse, Rene P.; Zaleska, Margaret M.; Moyer, John A.

CORPORATE SOURCE: Chemical Sciences CNS Disorders Divisions, Wyeth-Ayerst Research, Princeton, NJ, 08543-8000, USA
 SOURCE: Journal of Medicinal Chemistry (1998), 41(2), 236-246
 CODEN: JMCMAR; ISSN: 0022-2623

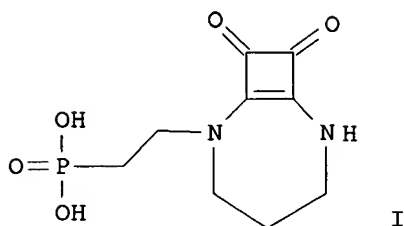
PUBLISHER: American Chemical Society

DOCUMENT TYPE: Journal

LANGUAGE: English

OTHER SOURCE(S): CASREACT 128:75452

GI



AB The diazabicyclic amino acid phosphonate I, [2-(8,9-dioxo-2,6-diazabicyclo[5.2.0]non-1(7)-en-2-yl)ethyl]phosphonic acid, was identified as a potent NMDA antagonist. It contains the α -amino acid bioisostere 3,4-diamino-3-cyclobutene-1,2-dione and an addnl. ring for conformational rigidity. I was as potent as CGS-19755 in the [3H]CPP binding assay, the stimulated [3H]TCP binding assay, and the NMDA-induced lethality model in mice. A single bolus dose of I, administered i.v. following permanent occlusion of middle cerebral artery (MCA) in the rat, reduced the size of infarcted tissue by 57%. Structure-activity relationship (SAR) studies have indicated that the six- and eight-membered ring derivs. had diminished activity and that the two-carbon side chain length was optimum for NMDA receptor affinity. Substitution on the ring was counterproductive in the case of sterically demanding di-Me groups and of no consequence in the case of an H-bonding hydroxyl group. Replacement of the phosphonic acid group by either a carboxylic acid or a tetrazole group was unproductive. The potent bicyclic NMDA antagonists were synthesized efficiently by virtue of their achiral nature and the ease of vinylogous amide formation from squaric acid esters. I, being a unique NMDA antagonist structural type with a favorable preclin. profile, may offer advantages over existing NMDA antagonists for the treatment of neurol. disorders such as stroke and head trauma. I is currently under clin. evaluation as a neuroprotective agent for stroke.

IT 144912-54-9P 144912-55-0P 144912-64-1P
 144912-65-2P 144912-66-3P 144912-69-6P

144913-00-8P 144913-01-9P

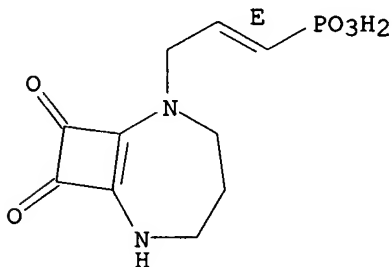
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)

(design and synthesis of [(dioxodiazabicyclononyl)ethyl]phosphonic acid as a potent NMDA antagonist via use of cyclobutenedione as achiral amino acid bioisostere)

RN 144912-54-9 CAPLUS

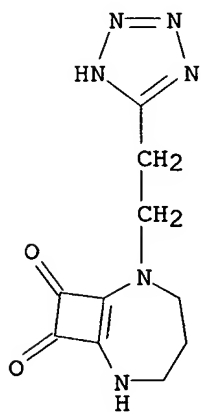
CN Phosphonic acid, [3-(8,9-dioxo-2,6-diazabicyclo[5.2.0]non-1(7)-en-2-yl)-1-propenyl]-, (E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



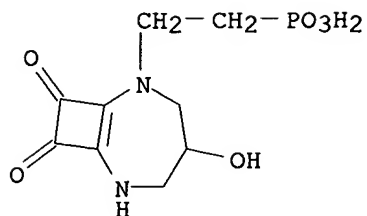
RN 144912-55-0 CAPLUS

CN 2,6-Diazabicyclo[5.2.0]non-1(7)-ene-8,9-dione, 2-[2-(1H-tetrazol-5-yl)ethyl]- (9CI) (CA INDEX NAME)



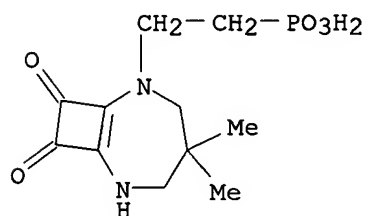
RN 144912-64-1 CAPLUS

CN Phosphonic acid, [2-(4-hydroxy-8,9-dioxo-2,6-diazabicyclo[5.2.0]non-1(7)-en-2-yl)ethyl]- (9CI) (CA INDEX NAME)



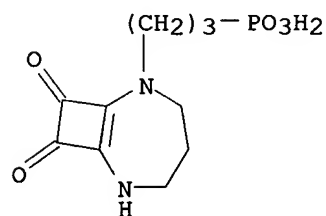
RN 144912-65-2 CAPLUS

CN Phosphonic acid, [2-(4,4-dimethyl-8,9-dioxo-2,6-diazabicyclo[5.2.0]non-1(7)-en-2-yl)ethyl]- (9CI) (CA INDEX NAME)



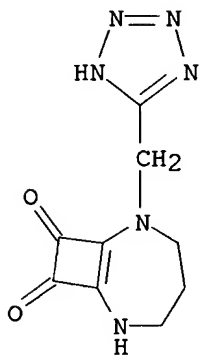
RN 144912-66-3 CAPLUS

CN Phosphonic acid, [3-(8,9-dioxo-2,6-diazabicyclo[5.2.0]non-1(7)-en-2-yl)propyl]- (9CI) (CA INDEX NAME)



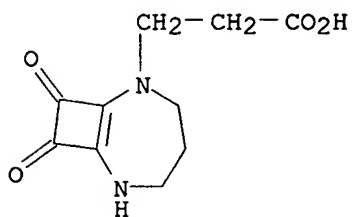
RN 144912-69-6 CAPLUS

CN 2,6-Diazabicyclo[5.2.0]non-1(7)-ene-8,9-dione, 2-(1H-tetrazol-5-ylmethyl)- (9CI) (CA INDEX NAME)



RN 144913-00-8 CAPLUS

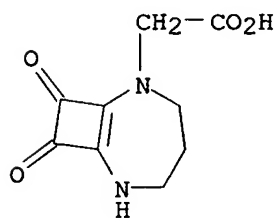
CN 2,6-Diazabicyclo[5.2.0]non-1(7)-ene-2-propanoic acid, 8,9-dioxo-, monosodium salt (9CI) (CA INDEX NAME)



● Na

RN 144913-01-9 CAPLUS

CN 2,6-Diazabicyclo[5.2.0]non-1(7)-ene-2-acetic acid, 8,9-dioxo-, monosodium salt (9CI) (CA INDEX NAME)



● Na

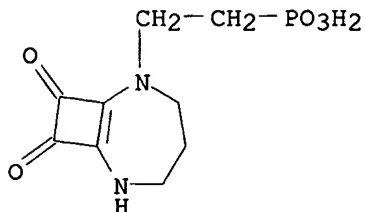
IT 144912-63-0P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(design and synthesis of [(dioxodiazabicyclononenyl)ethyl]phosphonic

acid as a potent NMDA antagonist via use of cyclobutenedione as achiral amino acid bioisostere)

RN 144912-63-0 CAPLUS

CN Phosphonic acid, [2-(8,9-dioxo-2,6-diazabicyclo[5.2.0]non-1(7)-en-2-yl)ethyl]- (9CI) (CA INDEX NAME)



IT 144912-83-4P 144912-87-8P 144912-92-5P

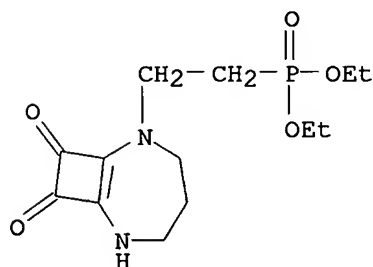
144912-99-2P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(design and synthesis of [(dioxodiazabicyclononenyl)ethyl]phosphonic acid as a potent NMDA antagonist via use of cyclobutenedione as achiral amino acid bioisostere)

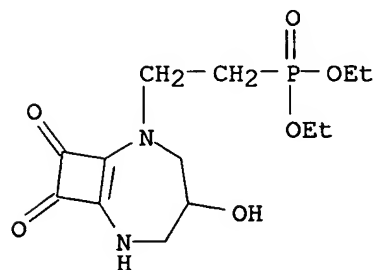
RN 144912-83-4 CAPLUS

CN Phosphonic acid, [2-(8,9-dioxo-2,6-diazabicyclo[5.2.0]non-1(7)-en-2-yl)ethyl]-, diethyl ester (9CI) (CA INDEX NAME)



RN 144912-87-8 CAPLUS

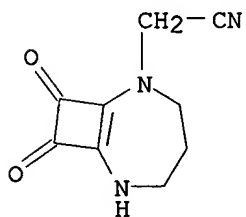
CN Phosphonic acid, [2-(4-hydroxy-8,9-dioxo-2,6-diazabicyclo[5.2.0]non-1(7)-en-2-yl)ethyl]-, diethyl ester (9CI) (CA INDEX NAME)



10/820,215

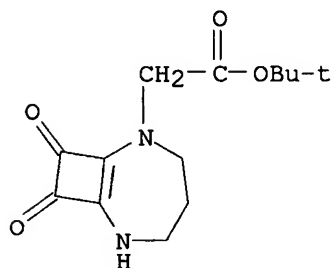
RN 144912-92-5 CAPLUS

CN 2,6-Diazabicyclo[5.2.0]non-1(7)-ene-2-acetonitrile, 8,9-dioxo- (9CI) (CA INDEX NAME)



RN 144912-99-2 CAPLUS

CN 2,6-Diazabicyclo[5.2.0]non-1(7)-ene-2-acetic acid, 8,9-dioxo-,
1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



REFERENCE COUNT:

38

THERE ARE 38 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

10/820,215

LI1 ANSWER 11 OF 17 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1997:5455 CAPLUS
DOCUMENT NUMBER: 126:74494
TITLE: Reaction of 3-morpholino-4-butoxy-3-cyclobutene-1,2-dione with amines
AUTHOR(S): Chen, Yizhao; Li, Jucai; Li, Wenzao; Yu, Lingzhuang; Hen, Linsen; Peng, Daquan
CORPORATE SOURCE: Dept. of Chemistry, Sichuan Univ., Chengdu, 610064, Peop. Rep. China
SOURCE: Sichuan Daxue Xuebao, Ziran Kexueban (1996), 33(3), 302-306
CODEN: SCTHAO; ISSN: 0490-6756
PUBLISHER: Sichuan Daxue Xuebao Bianjibu
DOCUMENT TYPE: Journal
LANGUAGE: Chinese

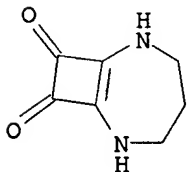
AB When 3-morpholino-4-butoxy-3-cyclobutene-1,2-dione (I) reacted with amines, the reaction products were different depending on the nature of amines and the reaction conditions. In general, aminolysis of ester group took place, amino groups entered into the ortho position of 3-cyclobutene-1,2-dione. When 1,3-diaminopropane or m-aminophenol reacted with I, transamination of squaraines in intramol. and intermol. occurred in addition to aminolysis. The products formed in the reaction of o-aminophenol and o-phenylenediamine with I were not 1,2- rather 1,3-substituted squaramides.

IT 66086-41-7P

RL: SPN (Synthetic preparation); PREP (Preparation)
(reaction of morpholino(butoxy)cyclobutenedione with amines)

RN 66086-41-7 CAPLUS

CN 2,6-Diazabicyclo[5.2.0]non-1(7)-ene-8,9-dione (9CI) (CA INDEX NAME)



L11 ANSWER 12 OF 17 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1993:39407 CAPLUS

DOCUMENT NUMBER: 118:39407

TITLE: Preparation of [[(2-amino-3,4-dioxo-1-cyclobuten-1-yl)amino]alkyl]carboxylic acid derivatives as N-methyl-D-aspartate (NMDA) antagonists

INVENTOR(S): Kinney, William Alvin; Garrison, Deanna Colette

PATENT ASSIGNEE(S): American Home Products Corp., USA

SOURCE: Eur. Pat. Appl., 33 pp.

CODEN: EPXXDW

DOCUMENT TYPE: Patent

LANGUAGE: English

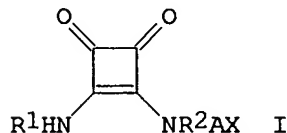
FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|------|----------|-----------------|------------|
| EP 496561 | A2 | 19920729 | EP 1992-300472 | 19920120 |
| EP 496561 | A3 | 19921223 | | |
| EP 496561 | B1 | 19950315 | | |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, PT, SE | | | | |
| US 5168103 | A | 19921201 | US 1991-806861 | 19911217 |
| IL 100679 | A1 | 19961031 | IL 1992-100679 | 19920116 |
| AU 9210301 | A1 | 19920730 | AU 1992-10301 | 19920117 |
| AU 639629 | B2 | 19930729 | | |
| ZA 9200358 | A | 19930719 | ZA 1992-358 | 19920117 |
| SK 280268 | B6 | 19991008 | SK 1992-144 | 19920117 |
| CZ 286407 | B6 | 20000412 | CZ 1992-144 | 19920117 |
| CA 2059704 | AA | 19920723 | CA 1992-2059704 | 19920120 |
| CA 2059704 | C | 20020716 | | |
| JP 04321654 | A2 | 19921111 | JP 1992-7385 | 19920120 |
| JP 3167770 | B2 | 20010521 | | |
| AT 119873 | E | 19950415 | AT 1992-300472 | 19920120 |
| ES 2071428 | T3 | 19950616 | ES 1992-300472 | 19920120 |
| RU 2039035 | C1 | 19950709 | RU 1992-5010645 | 19920120 |
| FI 9200261 | A | 19920823 | FI 1992-261 | 19920121 |
| FI 105551 | B1 | 20000915 | | |
| HU 61970 | A2 | 19930329 | HU 1992-192 | 19920121 |
| HU 215838 | B | 20000628 | | |
| KR 206055 | B1 | 19990701 | KR 1992-780 | 19920121 |
| US 5240946 | A | 19930831 | US 1992-875925 | 19920429 |
| PRIORITY APPLN. INFO.: | | | US 1991-644157 | A 19910122 |
| | | | US 1991-806861 | A 19911217 |
| | | | CS 1992-144 | A 19920117 |

OTHER SOURCE(S): MARPAT 118:39407

GI



AB Title compds. [I; R1 = H, (phenyl)alkyl; R2 = R1, alkenyl; or R1R2 = CH2CH2, CH2CR6R7CH2, CH2CR8R9CR10R11CH2; R6, R8, R10 = H, alkyl, OH; R7, R9, R11 = H, alkyl; A = alkylene, alkenylene; X = CO2R3, P(O)(OR4)OR5, 3,5-dioxo-1,2,4-oxazolidin-2-yl, 5-tetrazolyl; R3, R4, R5 = H, alkyl], were prepared Thus, H2NCH2CH(OH)CH2NH2 was treated with O(CO2CMe3)2 in MeCN to give H2NCH2CH(OH)CH2NHCO2CMe3. The latter was condensed with BrCH2CH2P(O)(OEt)2 using Na2CO3 in EtOH to give (EtO)2P(O)CH2CH2NHCH2CH(OH)CH2NHCO2CMe3. This was condensed with 3,4-diethoxy-3-cyclobutene-1,2-dione in EtOH to give 3-[N-[2-(diethoxyphosphinyl)ethyl]-N-(2-ethoxy-3,4-dioxo-1-cyclobuten-1-yl)amino]-2-hydroxypropyl]carbamic acid 1,1-dimethylethyl ester. This was stirred with HCO2H and the residue was refluxed with EtN(CHMe2)2 in EtOH to give [2-(4-hydroxy-8,9-dioxo-2,6-diazabicyclo[5.2.0]non-1(7)-en-2-yl)ethyl]phosphonic acid di-Et ester. This was refluxed with Me3SiBr in ClCH2CH2Cl to give [2-(4-hydroxy-8,9-dioxo-2,6-diazabicyclo[5.2.0]non-1(7)-en-2-yl)ethyl]phosphonic acid. The latter inhibited N-methyl-D-aspartate-induced lethality in mice with ED50 = 1.8 ng/kg.

IT **144912-54-9P 144912-55-0P 144912-63-0P**
144912-64-1P 144912-65-2P 144912-66-3P
144912-67-4P 144912-68-5P 144912-69-6P
144913-00-8P 144913-01-9P

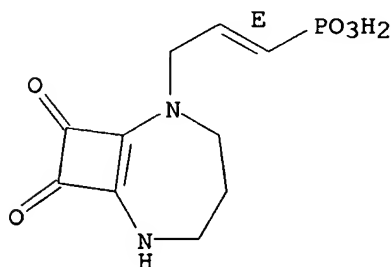
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of, as NMDA antagonist)

RN 144912-54-9 CAPLUS

CN Phosphonic acid, [3-(8,9-dioxo-2,6-diazabicyclo[5.2.0]non-1(7)-en-2-yl)-1-propenyl]-, (E)- (9CI) (CA INDEX NAME)

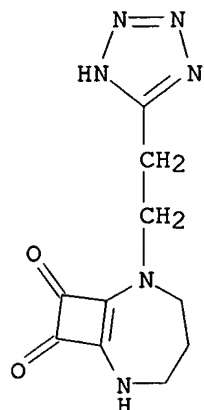
Double bond geometry as shown.

col. 17, line 66-67



RN 144912-55-0 CAPLUS

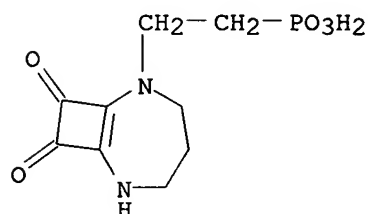
CN 2,6-Diazabicyclo[5.2.0]non-1(7)-ene-8,9-dione, 2-[2-(1H-tetrazol-5-yl)ethyl]- (9CI) (CA INDEX NAME)



RN 144912-63-0 CAPLUS

CN Phosphonic acid, [2-(8,9-dioxo-2,6-diazabicyclo[5.2.0]non-1(7)-en-2-yl)ethyl]- (9CI) (CA INDEX NAME)

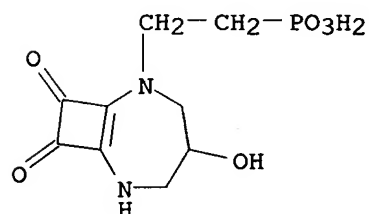
Ex 8



RN 144912-64-1 CAPLUS

CN Phosphonic acid, [2-(4-hydroxy-8,9-dioxo-2,6-diazabicyclo[5.2.0]non-1(7)-en-2-yl)ethyl]- (9CI) (CA INDEX NAME)

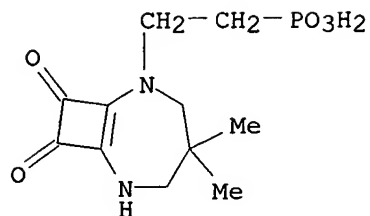
Ex 9



RN 144912-65-2 CAPLUS

CN Phosphonic acid, [2-(4,4-dimethyl-8,9-dioxo-2,6-diazabicyclo[5.2.0]non-1(7)-en-2-yl)ethyl]- (9CI) (CA INDEX NAME)

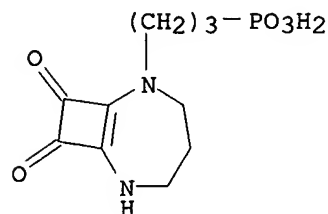
col. 17, line 50-52



RN 144912-66-3 CAPLUS

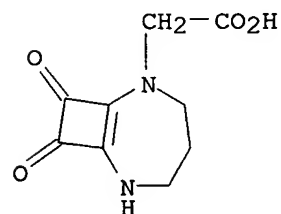
CN Phosphonic acid, [3-(8,9-dioxo-2,6-diazabicyclo[5.2.0]non-1(7)-en-2-yl)propyl]- (9CI) (CA INDEX NAME)

col. 17, line 57-59



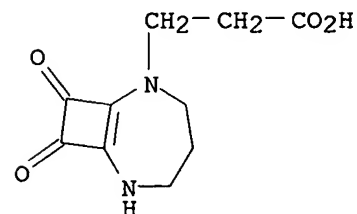
RN 144912-67-4 CAPLUS

CN 2,6-Diazabicyclo[5.2.0]non-1(7)-ene-2-acetic acid, 8,9-dioxo- (9CI) (CA INDEX NAME)



RN 144912-68-5 CAPLUS

CN 2,6-Diazabicyclo[5.2.0]non-1(7)-ene-2-propanoic acid, 8,9-dioxo- (9CI) (CA INDEX NAME)

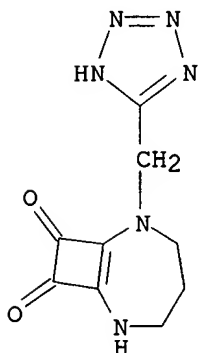


RN 144912-69-6 CAPLUS

CN 2,6-Diazabicyclo[5.2.0]non-1(7)-ene-8,9-dione, 2-(1H-tetrazol-5-ylmethyl)-

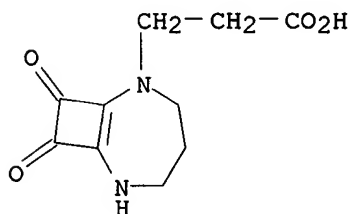
10/820,215

(9CI) (CA INDEX NAME)



RN 144913-00-8 CAPLUS

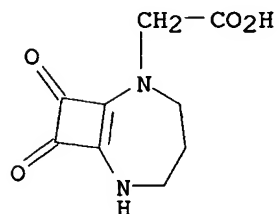
CN 2,6-Diazabicyclo[5.2.0]non-1(7)-ene-2-propanoic acid, 8,9-dioxo-, monosodium salt (9CI) (CA INDEX NAME)



● Na

RN 144913-01-9 CAPLUS

CN 2,6-Diazabicyclo[5.2.0]non-1(7)-ene-2-acetic acid, 8,9-dioxo-, monosodium salt (9CI) (CA INDEX NAME)



● Na

IT 144912-83-4P 144912-87-8P 144912-92-5P
144912-99-2P

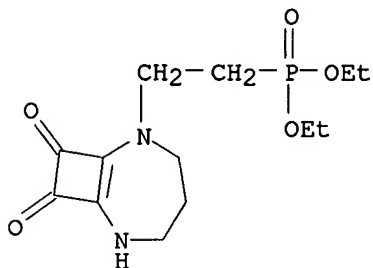
RL: SPN (Synthetic preparation); PREP (Preparation)

(preparation of, as intermediate for NMDA antagonists)

RN 144912-83-4 CAPLUS

CN Phosphonic acid, [2-(8,9-dioxo-2,6-diazabicyclo[5.2.0]non-1(7)-en-2-yl)ethyl]-, diethyl ester (9CI) (CA INDEX NAME)

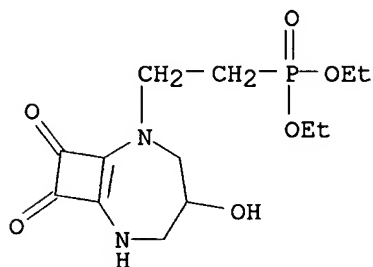
col. 15, line 54-55



RN 144912-87-8 CAPLUS

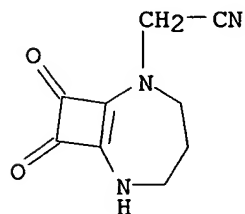
CN Phosphonic acid, [2-(4-hydroxy-8,9-dioxo-2,6-diazabicyclo[5.2.0]non-1(7)-en-2-yl)ethyl]-, diethyl ester (9CI) (CA INDEX NAME)

col. 17, line 16-17



RN 144912-92-5 CAPLUS

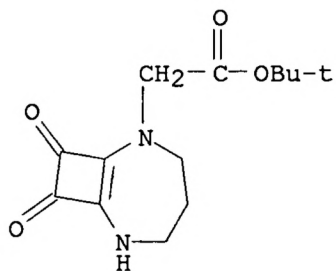
CN 2,6-Diazabicyclo[5.2.0]non-1(7)-ene-2-acetonitrile, 8,9-dioxo- (9CI) (CA INDEX NAME)



RN 144912-99-2 CAPLUS

CN 2,6-Diazabicyclo[5.2.0]non-1(7)-ene-2-acetic acid, 8,9-dioxo-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

10/820,215



~~III~~ ANSWER 13 OF 17 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1978:152588 CAPLUS

DOCUMENT NUMBER: 88:152588

TITLE: Ligand structure and complexation, XIV. Squaric acid and oxalic acid as building blocks of new crown ether amines and cryptands

AUTHOR(S): Voegtle, Fritz; Dix, Peter

CORPORATE SOURCE: Inst. Org. Chem. Biochem., Univ. Bonn, Bonn, Fed. Rep. Ger.

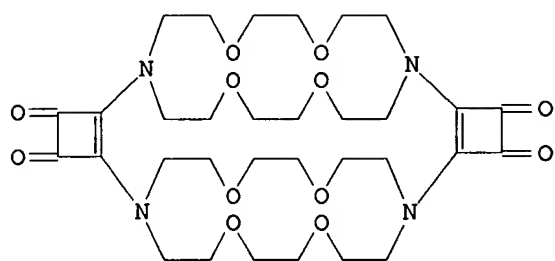
SOURCE: Justus Liebigs Annalen der Chemie (1977), (10), 1698-706

CODEN: JLACBF; ISSN: 0075-4617

DOCUMENT TYPE: Journal

LANGUAGE: German

GI



I

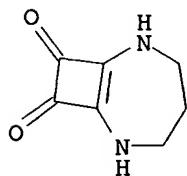
AB Aza crown ethers were prepared from squaric or oxalic acid and alkylenediamines or oxaalkylenediamines. I formed crystalline complexes with alkali metal ions.

IT **66086-41-7P**

RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)

RN 66086-41-7 CAPLUS

CN 2,6-Diazabicyclo[5.2.0]non-1(7)-ene-8,9-dione (9CI) (CA INDEX NAME)



10/820,215

111 ANSWER 14 OF 17 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1975:579022 CAPLUS

DOCUMENT NUMBER: 83:179022

TITLE: Synthesis of heterocyclic compounds by condensation of 5-chloro-2-aminobenzhydramine with C1-C2 reagents

AUTHOR(S): Roth, H. J.; Mensel, H.

CORPORATE SOURCE: Pharm. Inst., Univ. Bonn, Bonn, Fed. Rep. Ger.

SOURCE: Archiv der Pharmazie (Weinheim, Germany) (1975),

308(7), 557-63

CODEN: ARPMAS; ISSN: 0365-6233

DOCUMENT TYPE: Journal

LANGUAGE: German

OTHER SOURCE(S): CASREACT 83:179022

GI For diagram(s), see printed CA Issue.

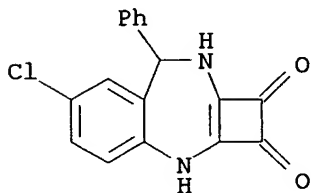
AB Condensation of 5,2-Cl(H₂N)C₆H₃CHPhNH₂ with RC(OEt)₃ (R = Me, Et), ClCOCOC₂H₄Cl, and 1,2-dimethoxycyclobutenedione gave quinazolines I, the macrocycle II, and the benzodiazepine III resp.

IT **57050-75-6P**

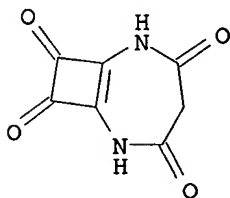
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)

RN 57050-75-6 CAPLUS

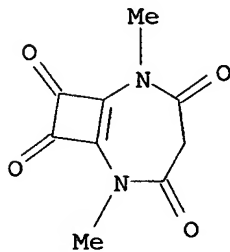
CN 1H-Benzo[e]cyclobuta[b][1,4]diazepine-1,2(3H)-dione, 6-chloro-8,9-dihydro-8-phenyl- (9CI) (CA INDEX NAME)



~~LI~~ ANSWER 15 OF 17 CAPLUS COPYRIGHT 2006 ACS on STN
 ACCESSION NUMBER: 1974:133399 CAPLUS
 DOCUMENT NUMBER: 80:133399
 TITLE: Polycarbonyl compounds. 7. Condensation of squaric acid 1,2-diamides with diethyl malonate
 AUTHOR(S): Seitz, G.; Morck, H.
 CORPORATE SOURCE: Chem. Inst., Tieraerztl. Hochsch. Hannover, Hanover, Fed. Rep. Ger.
 SOURCE: Archiv der Pharmazie (Weinheim, Germany) (1974), 307(2), 113-16
 CODEN: ARPMAS; ISSN: 0365-6233
 DOCUMENT TYPE: Journal
 LANGUAGE: German
 GI For diagram(s), see printed CA Issue.
 AB Condensation of the amides I (R = H or Me) with CH₂(CO₂Et)₂ (in the case of R = H in the presence of EtONa) at reflux gave the diazabicyclononenes II.
 IT **52094-04-9P 52094-06-1P**
 RL: SPN (Synthetic preparation); PREP (Preparation) (preparation of)
 RN 52094-04-9 CAPLUS
 CN 2,6-Diazabicyclo[5.2.0]non-1(7)-ene-3,5,8,9-tetrone (9CI) (CA INDEX NAME)



RN 52094-06-1 CAPLUS
 CN 2,6-Diazabicyclo[5.2.0]non-1(7)-ene-3,5,8,9-tetrone, 2,6-dimethyl- (9CI)
 (CA INDEX NAME)



~~1~~ ANSWER 16 OF 17 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1972:29271 CAPLUS

DOCUMENT NUMBER: 76:29271

TITLE: Spectroscopic and structural studies of some oxocarbon condensation products. V. Electronic structures of some cyclobuta[b]quinoxalines

AUTHOR(S): Griffiths, G. T.; Webb, G. A.

CORPORATE SOURCE: Dep. Chem. Phys., Univ. Surrey, Guildford/Surrey, UK

SOURCE: Journal of Molecular Structure (1971), 9(3), 333-42
CODEN: JMOSB4; ISSN: 0022-2860

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The electronic spectra of 12 cyclobuta[b]quinoxalines are reported and compared with electronic-transition energy and oscillator-strength values derived from Pariser-Parr-Pople MO calcns. The effects of nonplanarity on the electronic structures of these mols. are considered.

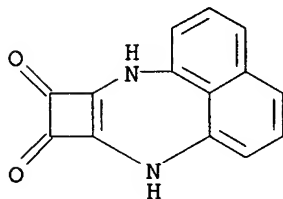
IT **33471-38-4**

RL: PRP (Properties)

(electron configuration and electronic spectrum of, structure in relation to)

RN 33471-38-4 CAPLUS

CN Cyclobuta[b]naphtho[1,8-e,f][1,4]diazepine-8,9-dione, 7,10-dihydro- (9CI)
(CA INDEX NAME)



~~11~~ ANSWER 17 OF 17 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1971:462688 CAPLUS

DOCUMENT NUMBER: 75:62688

TITLE: Spectroscopic and structural studies of some oxocarbon condensation products. IV. Spectroscopic and mass spectral investigation of some derivatives of squaric acid

AUTHOR(S): Griffiths, G. R.; Rowe, M. D.; Webb, G. A.

CORPORATE SOURCE: Dep. Chem. Phys., Univ. Surrey, Guildford/Surrey, UK

SOURCE: Journal of Molecular Structure (1971), 8(3), 363-71

CODEN: JMOSB4; ISSN: 0022-2860

DOCUMENT TYPE: Journal

LANGUAGE: English

AB PMR, vibrational, and mass spectral data for nine mols. derived from squaric acid substantiate the cyclobuta[b] quinoxaline structure for six of the mols., whereas the others are simple derivs. of squaric acid.

IT **33471-38-4**

RL: PRP (Properties)

(spectrum of)

RN 33471-38-4 CAPLUS

CN Cyclobuta[b]naphtho[1,8-e,f][1,4]diazepine-8,9-dione, 7,10-dihydro- (9CI)
(CA INDEX NAME)

